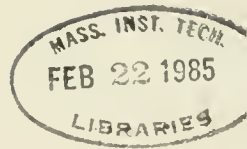


BASEMENT



Dowey

HD28
.M414
no. 1587-84
c.2



WORKING PAPER
ALFRED P. SLOAN SCHOOL OF MANAGEMENT

Formation and Early Growth of Biomedical and
Pharmaceutical Enterprises

Oscar Hauptman

WP1587-84

MASSACHUSETTS
INSTITUTE OF TECHNOLOGY
50 MEMORIAL DRIVE
CAMBRIDGE, MASSACHUSETTS 02139

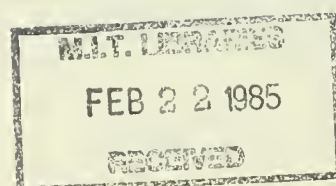
Formation and Early Growth of Biomedical and
Pharmaceutical Enterprises

Oscar Hauptman

WP1587-84

The research reported in this paper was in part supported by a grant from the Kaiser Family Foundation to the MIT Whitaker College Program in Health Policy and Management, and by funds from the RCA Corporation in support of the MIT David Sarnoff Professorship in the Management of Technology.

My gratitude goes to Professor Edward B. Roberts, Professor Stan Finkelstein, my colleagues at the Management of Technological Innovation Ph.D. Program, Kumar Nochur, Pieter Vanderwerf, John Friar and Marc Meyer, and especially to the entrepreneurs who shared their experience and insights with me.



<u>Contents</u>	<u>Page</u>
Abstract	1
Introduction	2
Research questions and hypotheses	7
Population, sample selection, data collection	17
Indicators and measures	28
<u>Empirical Results</u>	
Formation of biomedical and pharmaceutical enterprises: Founders and founding	32
Technology transfer to the small biomedical firm	39
Operating in a regulated environment: The interaction of technological innovation, risk associated with use, and the FDA regulations	46
Determinants of economic success of new biomedical firm	59
Brief agenda for future research.....	69
<u>References</u>	71
<u>Appendices</u>	
<u>Appendix A</u> : A sample of corporate names selected from the State House directory at stage 1 ("Phonetic search") .	75
<u>Appendix B</u> : Additional questions specific to the biomedical and the pharmaceutical industry	76
<u>Appendix C</u> : Sample attrition statistics (after stage 2)	82
<u>Appendix D</u> : Sample descriptive data	83
<u>Appendix E</u> : Criteria and examples for encoding ordinal data	84
<u>Appendix F</u> : Descriptive statistics of RAWU	86
<u>List of Tables</u>	
<u>Table 1</u> : Attrition of the initial sample during selection and data collection	26
<u>Table 2</u> : The legal status of the firms in the sample	27
<u>Table 3</u> : Comparison of profiles of biomedical and nonbiomedical entrepreneurs	34
<u>Table 4</u> : Education of the founder as a determinant of financing and performance of the firm	35
<u>Table 5</u> : Complementarity of founders' skills as a determinant of firm's commercial success	36
<u>Table 6</u> : MDs as founders of new firms: Their impact on firm's technology and performance	38
<u>Table 7</u> : Background of the founder and technological sophistication of the new firm	40
<u>Table 8</u> : Correlation between part-time involvement in founding the firm and its technological dimensions	41
<u>Table 9</u> : Sources of product ideas and technology, and the technological sophistication of the new firm	42
<u>Table 10</u> : The impact of contacts with the clinical environment on firm's technology and performance	44
<u>Table 11</u> : Technological relatedness of firm's products and its commercial success	45

<u>List of Tables</u> (Continued from previous page)	<u>Page</u>
Table 12: The impact of the FDA regulations and the risk associated with use of firm's products	49
Table 13: RAWU typical of the product area	49
Table 14: RAWU and the technological dimensions of the firm	50
Table 15: Professional background of the founders and the RAWU of firm's products	51
Table 16: Impact of the FDA regulations on product strategy of the firm by product area	53
Table 17: Impact of the FDA regulations on product strategy of the firm by product area(different grouping) .	53
Table 18: Use of indirect sales and their contribution to firm's revenues by product area	54
Table 19: Sales to industrial customers by product area	55
Table 20: Schedule of launching new products by biomedical firms in the sample	56
Table 21: Financial and performance indicators and the 1976 FDA amendment	57
Table 22: Financial and performance indicators and the 1976 FDA amendment; the transitory period of 1976-77	58
Table 23: Financial profile of biomedical enterprises ...	61
Table 24: Industrial and economic profile of biomedical firms	62
Table 25: The relation between financing and performance	63
Table 26: Multivariate regression: the impact of initial and subsequent financing on firm's economic performance	63
Table 27: Technological innovation and economic performance of the firm	64
Table 28: Technological innovation and mobilization of financial resources	65
Table 29: Dimensions of technological innovation and economic performance	65
Table 30: Average economic performance by firm's product area	66
Table 31: Multivariate regression: Determinants of economic performance of biomedical firms	68

List of Figures

Figure 1: The biomedical research spectrum	6
Figure 2: Path model of technology transfer to the new firm	43
Figure 3: The time sequence of the variables in the causal model of economic performance of biomedical firms	68

Abstract

This paper applies technological innovation theory to the process of formation and growth of biomedical and pharmaceutical firms. It is based on detailed data gathered from 26 firms, founded between 1968 and 1975 in the Commonwealth of Massachusetts. These data were supplemented by a three-member expert panel evaluation of the risk associated with use of firm's products.

Although the collected data addresses a wide range of issues, the main focus of the study was on the interaction between the medical and the technological attributes of the firm, and their impact on its survival and economic success.

The routes of technology transfer were traced, and the comparative impact of entrepreneurial professional experience, and the continuous flow of information to the firm were evaluated. In this context, the dominant role of the hospital and the medical school were elicited. Even weak contacts with universities and hospitals were found conducive to transferring technology from research to industry, enhancing technological innovation and transferring need data to the firms. All three transfers increased the firms' chances of commercial success.

A positive relationship was established between the level of technological sophistication of the firm and the risk associated with use of its products. Consequently, technological advancement of the firm has not necessarily resulted in high economic performance, in part because of the high demands put upon the firm's resources and time by the U.S. Food and Drug Administration approval process. Firms dealing with medical devices and pharmaceuticals were more sensitive to this regulatory process than those producing auxiliary products.

Enactment of the 1976 FDA regulations affecting medical devices was found to create a highly precarious environment for the marketing of new products. The impact of the amendment was found to be not limited only to its target product area, medical devices and supplies, but also challenged the management of firms producing drugs and pharmaceuticals.

Finally, the study suggests that the initial financial inputs have a threshold effect on subsequent economic performance of biomedical and pharmaceutical new firms. Unless these inputs reach the \$850,000 to \$1,000,000 mark (in 1970-1975 dollars), technological innovation would be negatively mediated by the risk associated with the use of firm's products and by the FDA quality control procedures. Consequently, these attempts at technological innovativeness will be detrimental to economic performance of new and underfinanced firms in the biomedical and pharmaceutical industry.

Introduction

Significant effort in the last decade to study the process of technological innovation has created a sound empirical and theoretical basis for its understanding and its effective management. The theory of technological innovation is not industry or technology specific, with only slight differentiation being made in the literature between technology-based industries such as semiconductors, computers, biotechnology, biomedical and pharmaceutical products, scientific and engineering instruments, and special manufacturing processes and materials, versus such basic industries as steel, textile, food, chemical industries, and agriculture.

Although the estimated volume of the U.S. biomedical and the pharmaceutical industry is quite significant, approximately 25 billion dollars in 1980^{*}, most of the research on technological innovation focus on other industries. Consequently, such industries as computers became the typical context of these studies. For instance Von Hippel (1977) studied the sources of innovation in the semiconductor and electronic subassembly processes, Freeman (1965) analyzed the R&D process in the electronic capital goods industry, and Tilton (1971) and Golding (as cited in Tilton, 1971) concentrated on the diffusion of technologies by using semiconductor technology as a case in point. Roberts(1968) studied the "spin-off" of new firms from

* Sources: Gibson R.B., D.R. Waldo, K.R. Levit, "National Health Expenditures 1982", Health Care Financing Review, Fall 1983, Vol.5, No. 1, pp.1-31; Predicast Forecast, Frost and Sullivan Press, NY, 1983.

MIT academic departments and laboratories, as well as government and industrial organizations. Knight (as cited by Von Hippel, 1982) used the data from the computer industry between 1944 and 1962 to describe the process of technological development. Research on innovations in scientific instruments (Von Hippel, 1977) and clinical chemistry analyzers (Von Hippel & Finkelstein, 1979) was more relevant to the biomedical industry, but it still did not address issues specific to it. More recently Horwitch (1982) presented biotechnology as a case in point of a field with high technological complexity.

Cross-industrial studies, when intended to present general observations, such as the state of the American economy (Lawrence & Dyer, 1983), or the process of international transfer of technology (Mansfield et al., 1982), suffer from the same bias of focus, with little or no reference to the biomedical industry.

Most of the studies that deal with the biomedical industry, either focus on diffusion of innovations as a two-stage communication process (Coleman, Katz & Menzel, 1966), or analyze exclusively the pharmaceutical industry and the influence of the FDA on its productivity and innovativeness (Ashford, Butler & Zolt, 1977; Young, 1982; Wardell, as cited in Roberts, 1981). Another direction of more relevant research focused on the changes in the pharmaceutical industry, historically analyzing the interaction between technology and the regulatory environment (Temin, 1979; Fuchs, 1974; Measday, 1977). They also address the economics of this industry. The analysis of medical innovations by Bernstein, Beaven, Kimberly, and Moch (1975, 79-114) focused solely on diffusion-relevant attributes of

medical technology.

Only a few studies address the complex issues of technological innovation in the biomedical industry. Comroe and Dripps (1977) rigorously analyzed the relation between basic research and its application in two areas of medicine. The Committee on Technology and Health Care of the National Academy of Science (1979) provided rich conceptual background for the analysis of equipment-embodied technologies but still insufficient empirical data. More recently, Homer (1983) analyzed the effect of government regulations on the emerging medical technologies, using a System Dynamics model.

The problem of insufficient research base, wanting both in scope and in rigor, might not be so severe if the empirical findings described above still apply to the biomedical industry. Putting it differently, although the theory of technological innovation has not been tested with empirical data from the biomedical industry, if this industry does not differ substantially from such industries as semiconductors or electronic instruments, we could assume that the theory will be still applicable to this context.

But is it really the case? Moskowitz, Finkelstein, Levy, Roberts and Sondik (1981) consider it to be indeed dubious. They caution the researcher of biomedical innovation from straightforward application of the theory to this setting: "In understanding the stages of technological development in health, we can best benefit from previous research in other fields by carefully examining health-related patterns rather than quickly accepting the

applicability of these findings to the health field" [our emphasis] (p.6).

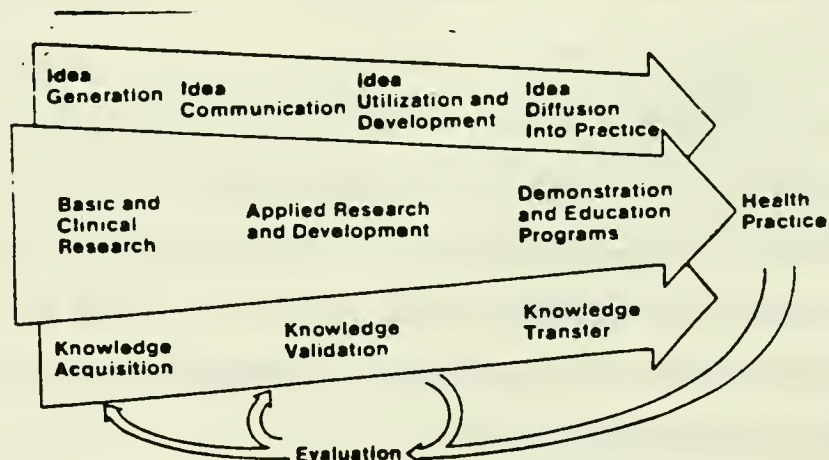
The question of transferability becomes more acute in the face of the numerous idiosyncracies, some of them quite significant, of the biomedical industry (Moskowitz et al., 1981: 6-7). First, the industry is extensively regulated by the federal government, namely by the Food and Drug Administration (FDA). The extent of this external interference and control of quality standards is overwhelming, to include both the efficacy and the safety of the product (pars. 510-515, FDA, 1976). The regulations also include directions about manufacturing and record keeping procedures (par. 501), and labeling and advertising standards (par. 502). Both sets of standards are much stricter than apply to nonbiomedical industries.

Second, the industry is supplying its products and technologies in a complex industrial goods market (Roberts, 1981), in which medical practitioners serve as intermediaries between producers and ultimate users - the patients. As has already been mentioned above, it was found that a two-stage communications and diffusion process operates in the biomedical industry (Coleman et al., 1966; Leonard-Barton, 1983). It should be noted that in this industry, relative to others, many practitioners have closer relationships with researchers because they have the opportunity to interact in their natural work environment - the hospital. This is especially true for those practitioners who are associated with academic medical center "teaching hospitals".

Third, the biomedical industry is an all encompassing name for a wide variety of products, embodying such scientific and engineering disciplines as biology, anatomy, microbiology, physiology, electronic and mechanical engineering, material and computer sciences, and many others. The various configurations of these disciplines present a wide range of proximity to the clinical "core" of the industry. It is not clear what proportion of biomedical firms produce diagnostic or therapeutic products of significance for the patient. How "medical" are these products, and to what extent are the idiosyncracies described above typical of them ?

The best that can be done is to combine "...empiricism largely from nonbiomedical fields with speculations on the transferability of ideas to the biomedical area" (Roberts, 1981: 51). The conceptual model presented by Moskowitz et al. (1981, 3-5) sets a structured research agenda for the biomedical field. This model (Figure 1) consists of two distinct processes - the progression of technology

Figure 1: The biomedical research spectrum (Roberts et al., 1981: 7)



from ideas to products and practices, and the interaction among people which facilitates this flow. The small and comparatively young biomedical firm, founded by an entrepreneurial individual or group, with the explicit objective of commercializing a product or technological knowhow, in addition to being interesting for the understanding of formation of new enterprises, also represents the junction of these processes. In the terminology of the conceptual model, the small firm contains all the stages of biomedical innovation, from idea generation, through its communication, utilization and development, and up to its diffusion into practice. As a research locus, the small firm should also contain sufficient data about most of the sources which influence innovations listed by Roberts (1981), such as staffing, idea generation and exploitation, and structural and strategic issues.

Ideally, this study should produce reliable causal predictors of success and failure of new biomedical enterprises, with clear description of the role of technological innovation in this process. Given the present size of the research base, this objective is not realistic. On the other hand, the identification of specific research questions pertaining to the biomedical industry, their transformation into testable hypotheses, and their initial test based on a small sample of young firms, are reasonable and worthwhile objectives.

Research Questions and Hypotheses

General

The theory of technological innovation contains several well articulated perspectives which provide specific descriptors of the

process. The perspectives which seem relevant both to the biomedical industry and to the specific setting of the small, newly founded enterprise are those of: a) technology-based entrepreneurship, and b) technology transfer. In addition, the studies of diffusion of medical technologies have generated empirical data pertaining to the process of technological innovation in the pharmaceutical industry, and its interaction with the FDA regulations. Consequently, we intend to link these areas of research by formulating research questions which are central to their interaction.

Background of the founders and founding the enterprise

Following the chronological order of events when founding a new enterprise, the social, educational, and professional backgrounds of technical entrepreneurs have been found to be quite specific, e.g., Forseth (1966), Goldstein (1967), Buddenhagen (1967), Roberts & Wainer (1968, 1971), Roberts (1968), Peters (1969), Taylor (1981).

According to the above studies, corroborated recently by the studies of industrial innovations in Sweden (Utterback et al., 1982), more than half of the technical entrepreneurs' fathers were self-employed, and the founders themselves had higher than average formal education. It should be noted that there was some variation between the studies: the entrepreneurs from Roberts' sample of MIT "spin-offs" have an average education of Master degree and higher, while Taylor's (1981) "spin-off" entrepreneurs from an industrial firm have the median formal education of B.Sc. plus one year. There are numerous findings concerning the family background of the entrepreneurs, e.g., higher probability of being a first-born son (Taylor, 1981), being

high on the need for achievement and low on need for power, or the religious distribution of the entrepreneurs and their fathers (Roberts & Wainer, 1971). None of these attributes was a reliable predictor of their success. The same studies present a clear profile of the entrepreneur at the stage of founding the new enterprise. Founding entrepreneurs have a median age between 32 (Martin et al., 1982) and 39 (Taylor, 1981), which corresponds to the mid-career phase of their life as defined by Schein (1981). At this stage the person is expected to "gain a measure of independence", to "carefully assess own motives, talents, and values...", to "carefully assess organizational and occupational opportunities as basis for making valid decisions about the next steps" (Schein: 42-43).

The motivation of the entrepreneurs to start their business is of explicit "egotistic" nature. "Salary" or "Financial reward", and "Being your own boss" were found to be the most important, and "Freedom to explore new areas", and "Challenge", the second most important motives (Roberts & Wainer, 1971; Taylor, 1981). Utterback et al. (1982) found that Swedish entrepreneurs, who started their firms with "positive" motives, such as "to be my own boss", or "to test a new idea", performed better than those whose motives were of a "negative" nature such as "my job came to an end".

Taylor (1981) presented numerous empirical data pertaining to the founding period. For instance, the period between contemplating and founding the enterprise and starting it, described by Van de Ven (1983) as gestation period, lasted nine years. Part-time participation was reported only by 26% of the entrepreneurs, lasting between 3 and 9

months, whereas earlier studies had found 50% part-time formation periods. Entrepreneurs had an average professional experience of approximately 15 years (Taylor, 1981; Utterback et al., 1982), consistent with their mid-30s age.

The most significant predictors of commercial success, stemming from founders' background and their attributes at founding, were: a) their formal education, with M.Sc.s, but not Ph.D.s, performing better than others; b) positive motives for starting the enterprise; c) the complementarity of skills of the co-founders, and larger number of co-founders. The research questions that follow naturally from the above findings are:

1. How similar are the biomedical entrepreneurs to their non-biomedical colleagues ?

2. How significant in the biomedical industry are the attributes that were conducive to success in nonbiomedical fields ?

The first research question will be addressed in a descriptive mode, by building a typical profile of the biomedical entrepreneur, and comparing it, on its face value, to the above mentioned data.

The second research question will be addressed through the following hypotheses:

H1: Enterprises founded by entrepreneurs having a second university degree perform better than those founded by entrepreneurs either with higher or lower degrees.

H2: High complementarity of co-founders' skills is conducive to better performance of their enterprise.

As a corollary to the above hypothesis, stemming from the findings by Bigelow (1982) about the generation and exploitation of ideas by research personnel in hospitals, it is interesting to test whether:

H3: Enterprises who had MDs among their co-founders performed differently than those without MDs.

Technology Transfer

The transfer of technology to the firm is another well articulated area of the theory of technological innovation. The perspectives relevant to the analysis of the biomedical industry include the informational links between basic research and industrial research and development. These were established by Comroe and Dripps (1977) to be vital in some instances for the biomedical industry. Allen (1977) presented specific findings concerning the patterns of communication of scientists and engineers. Lieberman (1978) analyzed the informational link operating through literature between physics and electronic engineering.

Mobility of personnel was found to be one of the most effective routes of technology transfer, both in the national and the international domains (Allen, Hyman, & Pinckney, 1983). The studies of "spin-offs" by Roberts (1968) and Taylor (1981) address the same issues, having found that the intensity of technology transfer from the previous employer of the founders to the newly founded firm has been conducive to its commercial success.

A different question is whether technological advancement of the firm and its products contribute to commercial success. Several studies (e.g., Marquis & Meyers, 1969; Rothwell et al., 1974) found that valid understanding of customers' needs, and product ideas that were generated from market inputs led to better economic performance at the product level than "technology-push" products. The importance of users as sources of product ideas as documented by Von Hippel (1977, 1982), contains direct implications for the potential role of the hospital in the biomedical industry.

Here, again, the transferability of the empirical findings to the biomedical industry is the big unknown. The research questions that should be asked are:

1. How important is the mobility of personnel from hospital and university research, from large biomedical firms, and from other technology-based or basic industries, for technology transfer to the new biomedical firm ?

2. How important is the hospital as the source of both product ideas and technologies, and of need data, for the small newly founded firm ?

3. How important is technology transfer to the biomedical firm to its commercial success ?

Considering the findings by Meyer (1982) that strategic technological focus was conducive to better economic performance in small firms in computer-related products markets, it is interesting to ask:

4. Is strategic technological focus of biomedical firms also conducive to their economic performance ?

The following hypotheses address most of the research questions above:

H4: The relevance and advancedness of the professional background of the founders influenced the technological sophistication of a firm's products.

H5: The relevance and advancedness of product ideas and the technology transferred to the firm enhanced the technological sophistication of firm's products.

H6: Contacts with hospitals are conducive both to technological sophistication of a firm's products and to commercial success of the firm.

H7: High technological sophistication of a firm's products does not necessarily result in its high economic performance.

H8: Strategic technological focus of the firm is conducive to its commercial success.

Technology, Risk Associated with Use, and the FDA

An important element of this study is the interaction between technology and risk associated with use (RAWU) of a firm's products, the influence of the FDA regulations on this interaction, and the resulting commercial performance of the firm. As mentioned above, there are less theoretical and empirical cursors to follow in studying these issues. The studies of innovations in the pharmaceutical industry (Ashford, et al., 1977; Young, 1982; The Committee on Technology and

Health Care, 1979; Bernstein, et al., 1975) present strong evidence for the significance of the interplay between regulatory constraints and innovativeness in this industry.

Wardell (1974) points to the fact that extensive regulations in the US decreased research productivity as measured by the number of new chemical entities (NCE) presented to the FDA for approval. He also showed (as cited in Young, 1982) that between 1962 and 1971 Britain led with respect to drugs available in both nations, calculated in terms of drug-years of prior availability. Britain also "...possessed nearly four times as many exclusively available drugs as did the United States" (Young, 1982, p. 19), mainly because the regulatory constraints there have not been as severe as in the US.

Moreover, "This over-regulation had increased drug industry costs, driven a great deal of research overseas or into safer generic areas, slowed or blocked the release of useful drugs"[our emphasis] (there). The amendment to the FDA Act in 1962 is described by Young (p.19) as "therapeutic disaster". Ashford, et al. (1977) voice the same sentiments with some reservation related to the complexity of cost-benefit analysis of the impact of the FDA regulations. They also suggest (p. 26) that "...the 1975 decision to accept foreign test data for efficacy certainly affects a pharmaceutical company's decision about where to conduct the testing".

Homer's study (1983) showed how sensitively a new medical technology's utilization could be influenced by government regulations. The simulated comparison between the regulated and the unregulated

environment encountered by a new implantable heart pacemaker technology shows that heavier regulations delayed product's technical evolution by one and a half years, and inhibited its sales growth during the first 12 (!) years after the new technology was introduced.

All these suggest that technological attributes of medical innovations are associated with the extent of FDA influence on their development. Important strategic implications for the biomedical firm also stem from the regulatory process, related to costs and schedules, product strategy, and possibly marketing strategy. A product's safety, or its inverse, the risk associated with its use (RAWU), is a strong determinant of the time and costs resulting from the federal approval process. Consequently, the financial requirements when founding a firm become quite substantial, needed to weather prolonged periods of commercial inactivity caused by the rigor of the FDA evaluation process.

The structure of FDA regulations partition the product areas of the biomedical industry into drugs and pharmaceuticals, medical devices, and para-medical products and supplies. The last two categories were first regulated by Congressional action in 1976.

The research questions that stem from the literature pertaining to pharmaceutical innovations are:

1. To what extent does the choice of product area, whether drugs and pharmaceuticals, medical devices, or products that are farther removed from the clinical core of the industry (dubbed by us "auxiliary products"), influence the subsequent

performance of the firms ?

2. What is the interaction between technological sophistication of the firm's products and the risk associated with their use ?

3. To what extent do the FDA regulations impact technologically novel biomedical products and the firms that generated them ?

FDA regulations appear to challenge significantly the management of biomedical firms. This leads to the question:

4. What are the strategic choices exercised by the management of biomedical firms to limit the FDA interference with their operations ?

Understanding the impact of new FDA regulations on specific product areas can significantly improve the evaluation of such initiatives in the future. The question that we could ask in the present context is:

5. What was the impact on the biomedical industry of the 1976 FDA amendment ?

The specific hypotheses related to the interactions among technology, RAWU and the impact of the FDA are:

H9: Technologically sophisticated biomedical products, especially those featuring first-of-a-kind or having special

specifications, will lead to high risk associated with their use.

H10: The impact of FDA regulations will be more significant for technologically novel biomedical products.

H11: Management of firms which operate in more extensively regulated product areas will have:

A. Greater concerns with appropriate selection of product strategy;

B. Marketing strategies that will attempt to decrease the sensitivity of the firm to FDA regulations.

H12: The regulatory environment for medical devices became more restrictive after the introduction of the 1976 amendment, lowering commercial performance of those firms which introduced their first products after 1976.

Finally, we should bear in mind that young firms are sensitive to the FDA regulations to such an extent that they will have serious problems in coping with their impact, especially in heavily regulated product areas. Consequently:

H14: A firm's commercial performance is influenced by its product area: performance of firms manufacturing drugs and pharmaceuticals will be lower than of those producing either medical devices or auxiliary products.

Population, Sample Selection, and Data Collection

The next step in the research was the selection of a relevant and controlled sample of biomedical firms, and the collection of data

pertaining to their formation and growth.

Population

Massachusetts has not been wanting of the relevant population - small, technology-based enterprises. Many of them were founded in the mid-seventies in the computer and other technology-based industries, that could exploit high level technological manpower produced by the universities in the area.

The growth in "Medical Instruments and Supplies" (SIC 384) reflects the national and the regional growth in high-tech industries, and is indicated by the following data:

1. The growth of Massachusetts employment in high-tech industries between 1975 and 1979 was almost twice the national figure of employment growth.

2. Although the number of the SIC 384 firms stayed almost constant, approximately one hundred, during this period, the average number of their employees increased by 57%, from 42 to 66 per firm.

It should be noted, though, that the situation in the biomedical industry differed from other high-tech industries in the following factors:

1. While the computer industry became more standardized, moving into process innovation and into competition by price, many medical products were still highly specialized and were produced on small scale (Hekman, 1980).

2. Consequently, the computer industry was seeking low production cost regions in the US and abroad, while, in contrast, the medical instruments industry has been drawn to major research centers for transfer of technology, for testing of new products, and for their marketing. Boston, due to such institutions as Harvard Medical School and several other medical schools, Massachusetts General Hospital, the Glaucoma Foundation, the Center of Blood Research, and many other medical research institutions, is possibly the most world-famous center of medical research.

3. According to Hekman (p. 39), "Branch plants generate only 35.4% of employment in medical instruments industry, compared with 63.4% in computers". Consequently, single employment small firms play a more important role for the former. In the Northeast, 37.6% of the medical instruments firms are single location employers, generating 36.2% of this industry's employment.

Another attribute of biomedical firms is their comparatively small size. The Massachusetts Division of Employment Security reported in 1979 a total of 105 firms producing medical instruments (as cited by Dorfman, 1982, p.63), 80% of which had 15 employees or less, being the smallest among the high-tech industries examined by her.

It should be noted that in contrast to the growth of the biomedical industry, the employment in "Drugs and Pharmaceuticals" (SIC 283) in the state dropped in the same period by 23%, from 3505 to 2693 (DES, as cited by Dorfman, p.29).

Sample selection

The sampling procedure used in this study differs to some extent from those used in similar studies of new firms (e.g., Roberts, 1968; Taylor, 1982; Utterback et al., 1983; Meyer, 1982). Although our sample was clearly purposive, we attempted to make it as complete as possible.

Our assumption was that the data pertinent to our study would be available from firms with several specific attributes. First, they should be approximately one decade old, to allow sufficient time since incorporation so that their commercial performance will be of a more stable pattern, after the initial start-up turmoil. On the other hand, to facilitate collection of first-hand data directly from the founders, the firms should not be older than 15-20 years, which could increase the probability of founders' death, relocation, or change of ownership since incorporation.

Second, the firms should be formed for the purpose of doing business in the biomedical or the pharmaceutical industry, to present a more focused picture about their operations in this specific area. Multi-product conglomerates clearly do not fit this requirement.

Third, the firms should be vertically integrated, to present as much as possible a whole picture of production from R&D to marketing. Consequently, the firm should preferably be a single site employer and an independent legal entity, not an R&D, manufacturing, or marketing outlet of a larger corporation. Adhering to the above criteria, the process of sample selection consisted of five stages.

Stage 1 - "Phonetic search"

Corporations were selected initially from the 1970 to 1975 Massachusetts State House incorporation records, choosing all whose names suggested either a medical, pharmaceutical, biological, or a general technical "connection". Their dates of founding would make them between 14 and 8 years old at the end of 1983. This stage of sample development was performed between September and December 1982 and yielded approximately 500 names.

Stage 2 - Review of objectives of incorporation

Those firms which either did not have the required vertical integration, were not initially incorporated in Massachusetts, or did not actually operate in the biomedical or the pharmaceutical industry were screened out on the basis of direct review of the original records of incorporation or their microfiche in the State House registry. These records provided additional information about the names and the private addresses of the founders or the lawyers who incorporated the firms. Although this information was usually incomplete, it was very useful for the extended search of founders of dissolved enterprises. This stage was performed in January 1983, eliminating approximately 80% of the initial selection of corporate names, leaving 106 candidate firms. Appendix A presents a selected sample of names initially drawn and the results of Stage 2 screening.

Stage 3 - The quest for founders

The detailed search for the addresses and telephone numbers of the founders was an unstructured effort, very much in the tradition of

the "private eye". The yellow pages, industrial directories, telephone directories, the New England Telephone Information Service and the lawyers of the firms were the main sources of information that were used. This process was performed in March-April 1983 and was repeated in October 1983, yielding the coordinates of approximately 60 firms or their founders. It should be noted that firms that had been dissolved were not eliminated from the sample, though they were extremely difficult to trace.

Stage 4 - Pilot study

The purpose of the pilot study was to test the modified questionnaire with the target population. The initial questionnaire that was used as the basis for consequent modifications was similar to those used by Roberts and Wainer (1971), Taylor (1981), and Utterback et al. (1982). The main factors that were tested were the time that was required to complete the questionnaire and the relevance and clarity of the new questions related to the medical context. See Appendix B for the questions that were added to the original.

The four interviews that were conducted during April and May 1983 precipitated several modifications in the content of the questionnaire (mainly elimination of unnecessary or unfocused questions). Also, because the average interview was between 4 and 5 hours long, the questionnaire was divided in two - a self-administered part, containing mainly well-structured and simple questions, and an interview questionnaire, containing unstructured or complicated issues which required real-time clarifications or explanations.

Stage 5 - Securing founders' agreement to participate in the study

The explanation by telephone of the purpose and the scope of the study gained the agreement of 36 founders (including the pilot study group) to participate in it. Attrition at this stage claimed another 24 potential "data points". The common explanation for not being willing to participate was "Don't want to talk". As much as the specific causes could be traced, they were usually "preoccupation with the current problems of the firm", or "the experience was too painful to walk through it again for research purposes". A couple of wives, concerned with their husbands' "health and happiness", successfully screened off the attempt.

Those obstacles produced difficulties in obtaining information about the comparative performance or the product area of the firms which dropped out of our sample at this stage. As far as we can tell attrition biases are not significant. It is possible that the attrition of firms which were dissolved, or encountered severe operational difficulties, was comparatively high. At least one firm was under FDA investigation and could not participate in the study for legal reasons. Drugs and pharmaceuticals were represented among the "drop-outs" (about 4-5 firms), but the distinction between medical devices and auxiliary products, based on the limited data in the objectives of incorporation, was more difficult to make. This stage was completed in November 1983, concurrently with the final search for founders still missing from our mail list. After that the sample was frozen, and data collection was initiated.

Data collection

Stage 6 - Self-administered questionnaire

Of the 32 founders (excluding the pilot study), to whom the questionnaires were mailed, another 7 dropped out for various reasons. Some of the reasons that were resiliently transmitted upon insistence: "I'm too busy with my clinical research in Boston University"; "The firm does not exist anymore"; "The questionnaire is too long"; "He does not have the time, and he doesn't want to talk" (secretary); "Although I'm willing to participate, I'm leaving for business negotiation to Europe till the end of March".

There are no specific patterns of sample attrition at this stage, although again our data about the comparative economic success of "drop-outs" is incomplete. We know that at least one firm has approximately 400 employees, and another is a successful producer of heart pacemakers. Two firms were active in the product area of drugs and pharmaceuticals and at least two were in auxiliary products. This stage was completed in December 1983.

Stage 7 - Interviews

The interviews took place "in the field" - usually in the Chief Executive Officer's office. The founders of firms that were dissolved were interviewed at their homes or at the offices of their present employer. Travel related to the interviews covered most of eastern Massachusetts. The farthest location was Hartford, CT. This stage was completed in February 1984.

Stage 8 - Data evaluation

At this stage three additional firms were screened out from the sample, two of them due to confounded background or inadequate data and another because it had actually been incorporated in the early sixties.

The data points included in the sample were somewhat uneven: for the analysis of entrepreneurial background and the initial period of founding the firm, 28 cases were used, while for the detailed causal analysis, only 26 cases were included. One of the 26 cases lacked the data about entrepreneurial background, early founding, and financing.

The final sample included three firms from the pilot study, for which the data were collected in a slightly different format. Two firms that were actually incorporated in 1968 and 1969 were included in the sample, as representative of the agglomerates of firms founded by the same founders between 1965 and 1975.

The bias introduced by the various non-respondents is mainly of underrepresentation of the firms which were either dissolved, acquired by large conglomerates, or relocated to other regions of the US. For instance one firm has been undergoing acquisition by a Texas corporation, another was under federal investigation by the FDA, two relocated to Florida and California, and two founders just recently died (see summary in Appendix C).

On the other hand, we would contend that the firms included in

the sample are representative of the population of medical instruments firms, as described by Dorfman (1982) and by Hekman (1980). As also can be seen from the above anecdotal information about the reasons for self-elimination from the study, the firms that were excluded were of a broad range of sizes and of economic performances.

The breakdown by year of incorporation of the sample selection and the data collection stages is presented in Table 1.

Table 1: Attrition of the initial sample during selection and data collection

Year of incorporation	Total	1970	1971	1972	1973	1974	1975
Initial sample	506	65	76	66	92	78	129
Stage 2 selection	106	13	19	20	13	9	32
Mailing list of questionnaires	36	5	5	7	4	6	9
Complete data collected	29	5	5	7	2	5	5

Note: A 1974 incorporated firm actually was a 1968, and a 1975 - a 1969 firm.

Stage 9 - Expert panel evaluation of "Risk associated with use"

Although the data collected from the entrepreneurs included indicators of risk associated with their products' use, it was decided, due to the importance of this variable for causal analysis, to use a panel of experts for its evaluation. The panel comprised three MDs in the early stages of their professional career, who, independently of each other, estimated the risk associated with use of each of firms' products. The dimensions that were evaluated by the panel included risk associated with use of the products to the medical personnel as well as to the patients, the invasiveness of the products, and their proximity to the clinical high impact area of the industry.

The use of a panel of experts is recommended for assessment of risk associated with use of novel technologies (Fischhoff, Lichtenstein, Slovic, Derby, & Keeney, 1982). The size of the panel (three members) corresponds to the recommendations of Libby and Blashfield, (1978) and Rohbaugh (1979), who showed that increasing the size of the panel beyond three members will offer only incremental improvements in its reliability.

The Sample

The sample of this study is probably more representative of the biomedical firms which existed in 1983, than of the firms which have been founded between 1970 and 1975. This assumption is based on the

Table 2: The legal status of the firms in the sample

Legal status of the firm	F r e q u e n c y	
	Number	%
Independent	17	65
Dissolved	4	15
Being acquired	3	12
Owned by another firm	2	8
Total	26	100

low number of firms that were dissolved in the present sample (see Table 2), which is much lower than the common death rate of new start-ups. On the other hand, the number of medical instruments firms that existed in 1979 (Dorfman, 1982) was 105, similar to the number of firms that were still in the sample after the second selection stage.

The legal status of the firms in the sample is presented in Table 2. Additional descriptive information about the firms in the sample, including their business classification, and their product areas are provided in Appendix D.

Indicators and Measures

Reliability

Being aware of the inherently low reliability of such concepts as risk associated with use, comparative advantages of the products, and other questions requiring individual evaluation, we resorted to the use of aggregates whenever it was possible. The following indicators are representative of this problem, and the method used to solve it:

1. The various attributes of each firm's products were evaluated by the entrepreneurs on quasi-Likert^{*} ordinal scales. To increase their reliability, aggregate indices of technological sophistication of a firm's products were computed by summing up the scores of the importance of "new technology or first of kind", "special purpose or special specifications", and "calibre of product or personnel" as competitive advantages of a firm's products. The reliability of the additive indices for each of the products of the firms was sufficiently high, measured by Cronbach's alpha^{*} (slightly higher than 0.50). Another method of aggregation to derive the

* For detailed discussion see:

Miller, D. C. (1983). Handbook of research design and social measurement (4th edition). Longman, NY & London; Novick, M. R., & Lewis, C. (1967). Coefficient alpha and the reliability of composite measurements. Psychometrika, 32, 1-13.

product specific technological index has been used by summing up the product specific scores on the above three scales, which were considered to be indicative of technological sophistication (alphas ranged between 0.50 and 0.60). The second level of aggregation, intended to derive the overall technological sophistication of the firm, was achieved by summing up the product specific indices of technological sophistication, yielding as expected a more reliable index ($\alpha=0.70$).

2. The assessment of risk associated with use of the products was supplied by the panel of experts as scores on quasi-Likert ordinal scales. We performed three level aggregation: first, the additive scale of the three members' scores yielded a Cronbach alpha of 0.91. Second, the additive scale of the scores on "Risk associated with use to the patient" and the "Invasiveness" for each product, yielded Cronbach's alphas between 0.92 and 0.96. Finally, the overall risk associated with use index of the firm was derived by summing up the product specific indices, to yield a Cronbach alpha of 0.98. After the above transformation of data, the resulting indices were treated as interval variables.

Ordinal scales

The prerequisites of quantitative analysis include at least ordinally scaled variables. For this purpose we performed ordinal scaling on the following variables, which were initially encoded in nominal categories:

1. Technological sophistication of entrepreneur's professional background. Entrepreneurs who presently or recently held predominantly R&D or research positions were encoded as "high" on this scale, and all the others were encoded as "low" (see Appendix E1 for relevant examples).

2. Relevance and technological sophistication of entrepreneur's industrial background. Entrepreneurs whose previous employment was predominantly or recently in universities or hospitals were encoded as "high" on this scale, those with medical or pharmaceutical industrial experience were encoded as "moderate", and the rest as "low" (see Appendix E2 for relevant examples).

3. Relevance and technological sophistication of sources of product technologies. Predominantly university and hospital-based sources were encoded as "high", those defined as "public domain" were encoded as "low", and the rest as "moderate" (see Appendix E3 for relevant examples).

4. Relevance and technological sophistication of sources of product ideas. Sources predominantly from universities, inventions, or from research consultants were encoded as "high", refinements of existing products or evolution from past work were encoded as "low", with the necessary correction for entrepreneur's professional and educational background, and the rest as "moderate" (see Appendix E4 for relevant examples).

5. Complementarity of founders' skills. Firms which had a mix of technical and business skills among its founders were encoded as "high", and the rest as "low" on this scale (see Appendix E5 for relevant examples).

Commercial success

Several studies in the past used quite simple indicators of commercial success of new firms. Meyer (1982) argued that growth of sales "proved unreliable because it is biased towards young, fast growing firms" (p. 43). He proceeded by dividing the growth in sales by the age of the firm, using an aggregate of the last two years, to smooth for annual fluctuations.

Taylor (1981, 15-16), following the pattern of all Roberts' prior studies of new firms, also used growth rates of sales as a measure of economic performance, although he partitioned his sample into "relatively successful" firms, "...if [they have] average sales growth that places [them] in the top half of the sample, and if [they have] been profitable in at least two of the past three years" (p. 15), and "relatively unsuccessful" if they have not. It should be noted, though, that Taylor's sample has a wide distribution of the start-up year: from 1960 to 1981. This factor presents acute problems of control for his study, especially for causal analysis. Meyer's sample spans only eight years of corporate birthdates (1968-1976), compared with six years span for most of the firms in the sample used in the present study.

The significance of firm's age as a determinant of its sales

was tested and the results could not reject the null hypothesis of no difference. On the other hand, to smooth temporary fluctuations of sales, we used the average of the annual sales between 1980 and 1983 as the indicator of firm's commercial success. This index was highly correlated with the 1983 market value of the firm, as estimated by the entrepreneur ($R=0.92$), with the average number of firm's employees for the same four years ($R=0.95$), and with the growth in annual sales ($R=0.95$), validating its possible use as a single measure of firm's success.

Outliers

The significance of any "high-powered" statistics, when we try to explain the variation in a dependent variable by the variation in the independent variable, is jeopardized by the presence of outliers. In our sample, two outliers were detected in both economic performance and financing intensity; they were defined by face value only, without a formal criterion such as a prespecified number of standard deviations from the mean. Consequently, any analysis which included the above variables has been checked for the influence of outliers on the magnitude of the correlation between them.

Empirical results

Formation of biomedical and pharmaceutical enterprises: Founders and founding

The first question posed in this study addressed the issue of transferability of nonbiomedical findings and theories to the biomedical industry by questioning the similarity of biomedical entrepre-

neurs to their nonbiomedical colleagues.

The initial results, summarized in Table 3, suggest that the answer to the above question is affirmative indeed. Biomedical and nonbiomedical entrepreneurs are quite similar, except for the following dimensions:

1. The modal degree field shifted naturally from engineering to natural sciences, though the high frequency of business degrees among the biomedical entrepreneurs is somewhat indicative of the managerial complexities of this industry.

2. The comparative number of articles published by the biomedical entrepreneurs indicates their more distinct research orientation. This is corroborated both by their comparatively high level of formal education, and by their professional experience, with 42% in R&D or research and 20% in hospitals or universities.

3. The biomedical entrepreneurs have taken fewer business courses and slightly fewer other courses since their last degree. The former can be explained by the higher proportion of entrepreneurs with formal business degrees.

4. The distribution of their religious background is very different from their nonbiomedical colleagues, with 18% Protestants, 50% Catholics, and 32% Jews, in comparison with Buddenhagen's internal entrepreneurs' (1967) 57% Protestants, 19% Catholics, and 13% Jews, 49% Protestants, 31% Catholics, and 20% Jews in Goldstein's (1967) study of industrial "spin-offs", or Forseth (1966) 50% Protestants, 25% Catholics, 17% Jews, and 8% Buddhists in MIT "spin-offs". Roberts (1968) confirmed these results in his study of "spin-offs". As a trial

Table 3: Comparison of profiles of biomedical and nonbiomedical entrepreneurs

Dimensions of Entrepreneur's Profile (medians)	Nonbiomedical studies of spin-offs				Biomedical sample
	Taylor (1981) N	Roberts (1968)	Forseth (1966)	Goldstein (1967)	
	23	216	12	39	28
Age at founding	39	36	35	36	36
Probability of being married	0.83	-	0.92	-	0.86
Education	BS + year	MS	MS+	BS+	MS+
Most likely field of degree	Engineering	-	-	-	Natural Sciences, Business
Work experience (years)	15.4	-	-	-	13.2
Family owns business	57%	50%	58%	48%	61%
Courses since degree	3.9	-	-	-	2.5
Business courses	4.7	-	-	-	1.4
Patents at or before last employer	1.8	-	-	-	1.2
Papers at or before last employer	2.4	-	-	-	8.1

in meta-analysis, the combined results of the above studies, weighted by their comparative sample sizes present the religious distribution of entrepreneurs as 52% Protestants, 26% Catholics, and 17% Jews.

Roberts (1968) showed that entrepreneurs who held a Master's degree performed better than either those with a first degree or lower, or those with a Doctorate. Our data do not support this curvilinear relation between degree level and commercial success. On the one hand, when the sample is partitioned into those who held Master's degrees and the others, the former performed better, especially on average sales between 1980-1983 (Table 4). On the other hand, when both the Masters and the Ph.D.s were grouped together they outperformed entrepreneurs who held lower degrees on average sales 1980-83 and have been more successful in mobilizing long-term capital.

Table 4: Education of the founder as a determinant of financing and performance of the firm

Dimensions of the firm	N	Masters versus others		High versus low degrees	
		Masters	Others	Masters & Ph.D.s	Others
		9	16	14	11
Initial equity		112K	57K	124K	25K
Long-term capital		1118K	910K	1689K	298K*
Average sales in first two years		223K	123K	174K	143K
Average sales between 1980 and 1983		4369K	1071K*	3724K	636K*
Market value in 1983		940K	240K	250K	189K

The table figures are means of the various dimensions; *t-test $p \leq 0.10$

Seventy percent of the entrepreneurs reported that motives which could be described as personal were the most important in precipitating the activities which led to the founding of new firms. In comparison, "Conditions on the last job" were chosen as the most important motives to start the business by 12%, and "Business opportunity" by 15% of the entrepreneurs. "Business opportunity" seems substantially more important than "Conditions on the last job"; it was mentioned as the second most important motive by 48% of the respondents, while the latter was chosen only by 15% of them.

More specifically, the motives to establish the firm included "Being your own boss", "Freedom to explore new areas", "Challenge", and "Financial reward" at the top of the list, quite similar to the previous studies (e.g., Roberts & Wainer, 1971, Taylor, 1981). It should be noted though that in our study the exploration of new areas ranked somewhat lower, and "Challenge" higher than in the studies mentioned above.

At founding, the biomedical entrepreneurs differ from their nonbiomedical counterparts mainly by the extent of their part-time involvement with the new firm. Seventy eight percent of them started their firm on a part-time basis, in comparison with only 26% part-time work in Taylor's (1981) study and 50% in most of the other previous studies. Entrepreneurs of both types contributed between 40 and 50 man-hours per week to the establishment of the new firm, excluding dissimilarity in intensity of start-up activities as a possible explanation. The difference in part-time duration is even more striking, with 3 to 9 months for nonbiomedical versus almost 30 months for biomedical entrepreneurs.

The number of founders per firm was approximately 2.5, equivalent to 2.6 for Taylor's spin-off entrepreneurs. The importance of a well balanced assortment of professional skills and experience at founding seems obvious. For instance, technical professionals without any business experience would be quite inadequate in dealing with costing, finance and the legal aspects of their business. On the

Table 5: Complementarity of founders' skills as a determinant of firms' commercial success

Complementarity of founders' skills	N	Product Attributes		Performance & Financing Dimensions		
		Calibre of product or personnel	Competitive price	Market value 1983	Average sales 1980-1983	Equity
High	15	15	14	13	13	14
Low	9	8	10	12	12	10
Z-scores		2.3	1.3	0.2	0.3	1.3
Mann-Whitney one-tail p		0.01	0.1	NS	NS	0.1

Table figures are mean ranks sums; positive Z-scores indicate higher mean ranks sum for firms with high complementarity of founders' skills. See statistical footnote next page.

other hand, a group of MBAs will lack technical understanding and technical contacts, both being necessary for innovation and success of a technology-based enterprise.

When we compare the performance of firms with complementarity of founders' skills, those with high complementarity fare somewhat better on most performance variables, though the only differences which are statistically significant are "Calibre of product or personnel", and "Price", as competitive advantages of firm's products, and the initial equity of the firm. All performance indices are higher, though, on average for firms with high complementarity of founders' skills.

Another interesting question is to what extent the participation of MDs influences firm's performance or its technological attributes.

According to the results presented in Table 6, MDs as entrepreneurs of new firms are associated with low performance as measured by average sales after approximately a decade of operation.

Statistical footnote: A brief explanation of the statistical data presented in Table 6 is in order. It is typical of the hypothesis testing procedure when we are looking for associations between an ordinal and a nominal variable. This situation renders the t-test incorrect. Consequently, we apply non-parametric tests such as Mann-Whitney (for comparison of two samples), or Kruskal-Wallis (for comparison of k samples). Both use analogous rank ordering of the dependent variables according to the comparative magnitude of the data. The ranks are aggregated in each categoric group and transformed to derive some known statistical distributions, normal Z-scores for Mann-Whitney, and Chi square for Kruskal-Wallis. Although the figures in Table 6 (also 7, 9, 10) are "synthetic", namely, mean ranks in each categoric group, we intentionally presented them to enhance some

On the other hand, they do facilitate technological innovation in the firm: its products incorporate newer technologies, have special specifications or are of higher calibre than the products of firms which had not been founded by MDs.

Table 6 : MDs as founders of new firms: their impact on firm's technology and performance

MDs as founders	N	P r o d u c t A t t r i b u t e s			Performance Dimensions	
		New techno- logy/first of kind	Special purpose or specs	Calibre of product or personnel	Average sales 1980-83	Market value 1983
No MDs	19	13	13	14	15	14
At least one MD as founder	5	17	17	13	8	13
Z-scores		-1.1	-1.3	0.1	1.7	0.1
Mann-Whitney one-tail p		NS	0.1	NS	0.05	NS

Table figures are mean ranks sums; positive Z-scores indicate higher mean ranks sum for firms with no MDs among their founders.

To summarize this section our results support the applicability to the biomedical field of nonbiomedical findings related to personal attributes of the founders and the initial goals and events at the founding of new biomedical firms. This fact should not mask the existing differences between the two fields, such as a more distinct research orientation of biomedical entrepreneurs, or their prolonged part-time involvement with the new firm, which might be facilitated by their employment in academic or research environments. In addition the findings about the optimal degree level for biomedical entrepreneurship, the inconclusive results about complementarity of founders' skills, and the special impact of

visualization of the raw data and the relations between the categoric groups. This explicit presentation is especially valuable when three or more categoric groups enforce a curvilinear pattern in the dependent variable. We should also bear in mind that non-parametric statistics are preferable for interval data containing sharp outliers, whose parametric treatment might inflate relations between variables.

entrepreneurs with medical degrees on their firms point to the idiosyncracies of biomedical entrepreneurship.

Technology transfer to the small biomedical firm

Technology transfer to the small firm takes place mainly in two forms: first, through personnel mobility, which carries the technological knowhow accumulated by the founders with their previous employers, during their education, and through their general experience. It can be described as a "spin-off" process, although in previous studies by Roberts and associates they used this term more specifically to describe transfer of technology from established technology-based organizations to new high-tech start-ups.

The second source of technology is the continuous flow of information from the firm's environment through both formal and informal channels, such as literature, personal contacts, professional conferences, vendors, users and suppliers. This area has been extensively researched and documented by Allen and associates. A comprehensive summary of relevant data is presented in Allen, Hyman and Pinkney, Table 7 (1983: 203).

Taylor (1981) showed that the knowhow gained at the previous employer of the founder was essential for the founding of the new firm. In our study 50% of the respondents indicated that their firm could not have been started without this technology; an additional 13% indicated that an important aspect of the company's work originated at the previous employer (48% and 17%, respectively, in Taylor, 1981).

When we tried to trace the influence of the entrepreneur's background on the technological sophistication of firm's products, the following three components emerged as the most salient:

1. The technological sophistication of the entrepreneur's professional background,
2. The relevance and the technological sophistication of entrepreneur's industrial background, and
3. How important was the technology transferred to the firm for its establishment and operations. This variable actually represents the intensity of the link between the technology of the "parent" firm or firms and the new enterprise.

Table 7: Background of the founder and technological sophistication of the new firm

Technological attributes of the firm	P r o f e s s i o n a l b a c k g r o u n d		Technological sophistication of industrial background		
	Not in R & D	In R&D or research	Low	Moderate	High
	N 10	13	9	9	5
New technology or first of kind	11	13 (NS)	12	10	16 (NS)
Special purpose or specifications	11	13 (NS)	11	10	17 *
Calibre of product or personnel	14	11 (NS)	10	12	16 (NS)

* Mann-Whitney and Kruskal-Wallis tests: $p \leq 0.10$. The table figures are mean ranks sums; higher mean ranks indicate higher average score on a technological attribute of the firm.

The results presented in Table 7 are in the hypothesized direction, though most of them are not statistically significant. It is reasonable to assume that the background of the founder is not directly associated with the technology of the firm. The intensity of technology transfer however proved to be positively correlated with

two of the technological attributes of firm's products, embodying a new technology or being first-of-a-kind, and the perceived calibre of the product or of firm's personnel, with statistical significance of $p \leq 0.08$ and $p \leq 0.06$, respectively.

The next step was to derive an index of technology transfer by multiplying the three components discussed above. The index, which was treated as continuous and interval, correlated with the technological sophistication of the firm with statistical significance: Pearson $R=0.49$ ($N=26, p \leq 0.008$). The index which comprised only the two background variables but not the intensity of technology transfer to the firm produced only $R=0.13$. This regularity was also maintained for the average calibre of a firm's products or personnel: $R=0.31$ with the overall technology transfer index, but only $R=0.09$ with the background index, when the intensity of technology transfer was excluded.

Table 8: Correlation between part-time involvement in founding the firm and its technological dimensions

Technological Dimensions of the firm	N	Duration of part-time involvement in founding the firm
Technological sophistication of:		
First product	26	0.50**
Second product	20	0.23
Third product	16	0.13
The firm (products average)	26	0.54**
Entrepreneur's background	23	0.42*
Technology "spin-off"	21	0.49*

Table figures are Pearson correlations; * $p \leq 0.05$; ** $p \leq 0.005$

Another aspect of the technology transfer process is revealed by our data concerning part-time involvement in the firm's activities by these biomedical entrepreneurs (Table 8). It seems that technologically more sophisticated products either required more

preparatory time for R&D activities, or they were generated and exploited by entrepreneurs whose work environment permitted sufficient slack for their activities related to founding the new firm. In the face of our data related to the "spin-off" process of technology transfer, the latter explanation seems more plausible.

The second source of a product's technological attributes is the continuous flow of product ideas and technologies to be embodied in the final product. The data presented in Table 9 show that advanced sources of product ideas and technologies enhance technological innovation in a firm's products, though again the separate statistics for each of the source components are insignificant. Following a procedure similar to the one applied to the indicators of the technological "spin-off" (Table 7), we derived the multiplicative index of continuous technological flow, which correlated with the firm's technology by $R=0.32$ ($N=24, p \leq 0.005$), and with the duration of part-time involvement of the founders by $R=0.36$ ($N=23, p \leq 0.05$).

Table 9: Sources of product ideas and technology, and the technological sophistication of the new firm

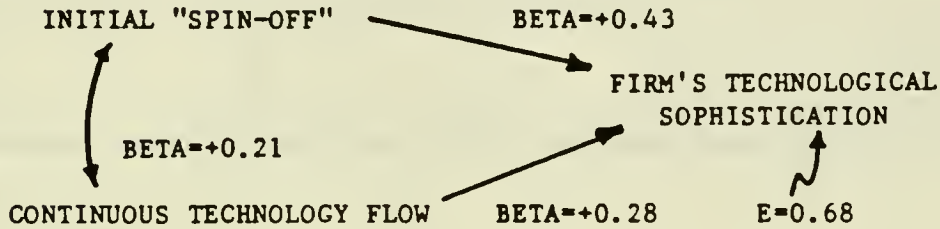
Technological attributes of the firms	Technological sophistication and relevance of product ideas			Technological sophistication and relevance of product technologies		
	Low N 10	Moderate 9	High 7	Low 15	Moderate 5	High 6
New technology or first of kind	14	5	19*	9	15	9*
Special purpose or specifications	13	13	15(NS)	12	12	17(NS)
Calibre of product or personnel	13	9	18(NS)	12	12	17(NS)

Kruskal-Wallis test: $*p \leq 0.01$. The table figures are mean ranks.

To complete the causal analysis of technology transfer, or in

other words to trace the comparative importance of the two sources of technology for the technological advancement of the firm, we used

Figure 2: Path model of technology transfer to the new firm



multivariate regression analysis. The indices shown in the path analysis model presented in Figure 2 indicate that the two sources complement each other in transferring technology to the new firm. The regression coefficients for both sources are statistically significant, and the resulting $R^2=0.32$ is quite high for this type of data.

The impact of the continuous flow of technology on the firm is somewhat weaker than the initial "spin-off" transfer by the founders. Interestingly the results of the multivariate regression for the first product of the firm emphasize the role of the initial "spin-off" process ($R^2=0.26$, $BETA=0.53$), at the same time rendering the second source of technology statistically insignificant. The same results were obtained when the outliers are excluded: only the initial source of technology was still statistically significant ($R^2=0.25$).

The role of the clinical environment, hospitals and medical schools, as a source of continuous flow of technology and product ideas to the firm, cannot be exaggerated. According to Allen (1977),

Table 10: The impact of contacts with the clinical environment on firm's technology and performance

The number of clinical contacts	N	P r o d u c t A t t r i b u t e s			P e r f o r m a n c e D i m e n s i o n s	
		New techno-logy/first of kind	Special purpose specs	Calibre of product or personnel	Average sales 1980-83	Market value 1983
No clinical contacts	7	9	9	12	11	11
At least 1 clinical contact	19	15	15	14	14	14
Z-scores		2.0	1.8	1.6	0.8	0.8
Mann-Whitney one-tail p		0.02	0.03	0.05	NS	NS

The table figures are mean ranks sums. Positive Z-scores indicate a higher mean ranks sum for firms with at least one clinical contact.

informal contacts are essential for this process to take place.

Although we have already addressed this issue through the path model of technology transfer by ranking hospitals and medical schools at the top of the technology sources scales, we used the data about informal contacts of the entrepreneurs with their environment to elicit the strength of these contacts.

The results in Table 10 are overwhelmingly in the hypothesized direction, showing that firms which maintained even weak contacts with the clinical environment developed products that incorporated newer technologies and/or special specifications, and were of high perceived calibre. They also performed somewhat better economically, though the difference was not statistically significant. These results corroborate our technology transfer model, as well as our ordering of the industrial relevance to the new biomedical firm of the entrepreneur's background. On the other hand, it becomes clear that the commercial performance of the firm is determined to a lesser extent by these factors.

Although our data do not focus on managerial strategy of the firm concerning R&D, the issues raised by Meyer (1982) still can be

Table 11: Technological relatedness of firm's products and its commercial success

Between:	Pearson correlations between technological sophistication of firm's products		
	Total (N) sample	High performance (N) firms	Low performance (N) firms
First and second products	(20) 0.73***	(13) 0.77***	(7) 0.64*
First and third products	(16) 0.31	(11) 0.56**	(5) -0.54
Second and third products	(16) 0.52**	(11) 0.64**	(5) 0.13

Pearson correlation coefficients: *** $p \leq 0.001$; ** $p \leq 0.01$; * $p \leq 0.05$

addressed. He suggested that technological and marketing strategic focus of the firm will enhance its economic performance, actually prescribing concentration on specific core technologies and markets, instead of hedging. We used the aggregated technological indicators of each firm's products to test the above hypothesis.

It is clear from Table 11 that strong relations exist between the degree of technological sophistication of chronologically consecutive products of the firm. These ties are much stronger for adjacent products than between products 1 and 3. Furthermore, firms which performed economically better, as measured by their average 1980-1983 sales, are more technologically focused than firms with low performance.

It should be noted that our results are only tangentially comparable to Meyer's: he analysed the firm's focus on specific

technologies, while we tested the influence of the pace of technological innovation, implicitly assuming that it takes place in the frame of specific core technologies.

Our data related to technology transfer to the new biomedical firm implies that although this process contains familiar components, such as the background of the entrepreneur and the "spin-off" effect, it is quite specific to the biomedical field. First, the hospital and the medical school seem to be important sources of new product ideas and advanced product-embodied technologies. Second, the lag between founding the firm and its full fledged operations is longer in comparison to the nonbiomedical firms, especially for those with more advanced products. On the other hand, it seems that high technological sophistication does not by itself determine commercial success. As was mentioned above, the impact of the FDA regulations is presumably stronger on novel and technologically advanced products, which might reduce their source firm's economic performance. The next section of the paper directly addresses these issues.

Operating in a regulated environment: The interaction of technological innovation, risk associated with use, and the FDA regulations

Before we address the main issues of this section, dealing with the causal relations between technology, risk associated with product use, and the impact of the FDA regulations, it is important to understand the various dimensions of the FDA requirements which bear upon the biomedical firm.

Sixty five percent of the products of the firms in our sample were regulated by the Bureau of Medical Devices of the FDA and 27% by either the Bureau of Drugs or Biologicals. Only two firms considered themselves not being regulated at all, either because they launched their products (medical devices or auxiliary products) before their inclusion in the FDA regulations, or because their products were quite removed from the clinical and consequently the regulated core of the industry.

The entrepreneurs reported that the FDA regulations influenced their product strategies on the average 3.2 points on a 5-point scale (64%), and their impact on the firm in general, as measured by the number of operational issues impacted by the regulations, 2.8 points on a similar scale (56%). Forty two percent reported that the regulations were prone to inconsistent interpretations of the FDA examiners, and 19% reported that their products were actually misclassified by these examiners into wrong categories, probably due to insufficient FDA professional understanding.

The medical devices and auxiliary products in our sample were mostly of classes I and II (86%), which require nonclinical proof of safety and efficacy, while 14% were of class III, requiring clinical tests. The former products were usually approved in the frame of paragraph 510K of the 1976 amendment, which is known in the industrial jargon as the "510K form". The firms had to wait on the average between 45 to 90 days for the "approval from Washington", though for the most of the firms (62%) the process did not take more than 45 days. The approval process for class I and II products usually did not

require more than one iteration, initiated usually by the FDA examiners due to some missing data, product misclassification or simply lost correspondance.

The climate for the pharmaceutical and the biological products is much more restrictive. The approval of the investigational new drug (IND) application for preliminary tests of efficacy takes between two and five years. The premarketing approval of a new drug application (NDA) has been of similar magnitude, resulting together with the IND in 6 to 10 years of iterative testing and application.

The reported out-of-pocket expenses for external consultants, costs of clinical tests, special facilities or labeling procedures and other similar costs, range from none to \$120,000 per annum, with a \$30,000 median. We assume that neither figure includes lost revenues caused by the delays, nor the time spent by the founders.

At this stage it is interesting to know whether the above intervention by the federal authorities has been warranted by real issues of safety and efficacy of the products. Although our data do not address the cost-benefit analysis of government regulations, we tested whether products which were evaluated by the experts panel as having high RAWU drew more "fire" from the FDA (see Appendix F for descriptive statistics of the RAWU). The data presented in Table 12 support the overall validity of at least the direction of the FDA intervention. The correlation between RAWU and the impact of the FDA regulations on the firm, as measured by the RAWU of its products, is statistically significant. It seems logical that the impact of first

Table 12: The impact of the FDA regulations and the risk associated with use of firm's products

Risk associated with use of firm's products	The overall impact of FDA regulations		Expenses for the FDA interface	
	N	R	N	R
First product	26	0.35**	19	0.20
Second product	19	0.29	15	0.32
Third product	16	0.14	13	0.51**
The firm (products average)	26	0.32*	19	0.47**

Spearman and Pearson correlations: * $p \leq 0.1$; ** $p \leq 0.05$. Seven entrepreneurs could not evaluate their FDA interface expenses.

product's RAWU was the most significant: a false start might have been critical for a new firm. On the other hand, the increasing correlations between the FDA generated expenses and the RAWU of products 2 and 3 is hard to explain. We would hypothesize that most of the FDA expenses related to the first product were perceived by the interviewed entrepreneurs as founding expenses, while the expenses related to the second and third products were perceived as operational, and were reported as such.

Table 13: RAWU typical of the product area

Risk associated with use of firm's products	P r o d u c t A r e a			
	Auxiliary products	Medical devices	Drugs and pharmaceuticals	p of stat. signif.
N	6	14	6	
First product	22	11	12	0.005
Second product	15	8	8	0.05
Third product	14	7	7	0.1
The firm (products mean)	22	11	11	0.005

The table figures are mean rank sums. Higher sums indicate products with lower RAWU.

As we already know, the FDA regulations are much more restrictive for drugs and pharmaceuticals than for medical devices and auxiliary products. To what extent is this quality control effort warranted by the differences in RAWU, inherent to these product areas? The answer to this question is affirmative: the expert panel rating of

RAWU, typical of each product area shows (Table 13) that the FDA differential emphasis is well grounded.

The interaction between technological innovation, RAWU, and the impact of the FDA, is another area of interest for the biomedical

Table 14: RAWU and the technological dimensions of the firm

Technological dimensions of the firm	Risk associated with use of :		
	First product	Second product	Third product
N	26	20	16
New technology or first of kind	0.34**	0.45**	0.33*
Special specifications or special purpose	0.06	0.09	0.06
Calibre of product or personnel	-0.14	0.10	-0.18

Pearson correlations: * $p \leq 0.10$; ** $p \leq 0.05$. Positive correlations indicate association of high RAWU and high score on the technological dimensions.

industry. According to our findings, products with high RAWU were developed by technologically advanced firms (Table 14). Special specifications or special purpose of firm's products were less correlated with RAWU, and the relation with calibre of product or personnel is quite unstable and statistically insignificant.

The last finding brings us to the next issue: as we have shown in the previous chapter, the "spin-off" process effectively transfers technology to the new firm. The main determinants of technological advancement of the firm are the previous positions and industrial background of the founders. It is reasonable to assume, especially in the face of the relation between RAWU and the firm's technology, that the background of the founders might influence the RAWU of their

firm's products. The results summarized in Table 15 do not support this hypothesis. A possible explanation for these results might be that entrepreneurs with industrial experience that was unrelated either to the biomedical or to the pharmaceutical industries were less aware of the importance of this factor (RAWU), consequently designing products whose technological level did not justify their comparatively high RAWU.

Table 15: Professional background of the founders and the RAWU of firm's products

R A W U of the	N	Technological sophistication and relevance of						
		Industrial background			p	Positional background		p
		Low	Moderate	High		Not R&D	R&D	
First product	23	13	9	16	NS	9	14	0.04
Second product	16	8	7	15	0.10	7	10	0.08
Third product	13	7	6	13	NS	6	8	NS
The firm	23	12	10	16	NS	9	14	0.10

The table figures are mean ranks sums. High mean rank sums indicate products with lower RAWU.

At this stage we have succeeded in establishing the link between RAWU and the impact of the FDA regulations, and between RAWU and the technological dimensions of the firm. It is interesting to test to what extent RAWU and technology are the two sides of the same coin, whether one is the inverse of the other. The relations between the technological dimensions of the firm and the impact of the FDA regulations on the firm are only slightly supportive of this hypothesis: firms whose products embodied new technologies or were first-of-a-kind spent more than others on the FDA interface ($R=0.34, N=19, p \leq 0.08$). On the other hand, "special specifications or special purpose", and "calibre of product or personnel" were quite independent of the FDA's impact. The overall technological index of the firm, which consists of the above dimensions, was positively

correlated with the FDA expenses ($R=0.20$), albeit not statistically significant. These interferences with a firm's operations, in addition to what we already know about the delays precipitated by the FDA approval process, present significant obstacles for survival and success of the new biomedical and especially the pharmaceutical firm. What were the strategic and the operational measures applied by management to reduce the sensitivity of their firms to this interference ?

We assumed that a natural response could be higher awareness of the salience of product strategy, and consequently, more careful planning in the face of a more regulated environment. As drugs and pharmaceuticals are presumably more regulated than medical devices and auxiliary products, we assumed that the firms producing these products will report higher awareness or stronger impact of the FDA regulations on their product strategy.

The first indicator of managerial awareness of higher risk associated with developing regulated products was the strong association between estimated commercial risk of launching these products and the extent to which these product areas were regulated. Medical devices and drugs and pharmaceuticals were perceived as much riskier undertakings than auxiliary products (Kruskal-Wallis test's significance of $p \leq 0.04$). This relation was corroborated by the correlations between the RAWU and the estimated commercial risk of firm's products, which were statistically significant for the first product (Stearman $R=0.45$, $N=26$, $p \leq 0.01$) and for the firm, measured as an average of its products ($R=0.36$, $N=26$, $p \leq 0.05$). This correlation

for the second and the third products is also positive ($R=0.21$ and $R=0.22$, respectively).

Table 16: Impact of the FDA regulations on product strategy of the firm by product area

Impact of the FDA regulations	P r o d u c t a r e a					
	Auxiliary products		Medical devices with aux. prods.		Drugs or pharma. with others	
	%	(N)	%	(N)	%	(N)
Low	33	(2)	43	(6)	0	(0)
Moderate	0	(0)	21	(3)	33	(2)
High	67	(4)	36	(5)	67	(4)
Total	100	(6)	100	(14)	100	(6)

The data presented in Table 16 is congruent with the above results, though the relation between the impact of the FDA on product strategy and the product area of the firm is not strong enough to reject the null-hypothesis. Still $\text{Gamma}=0.17$, the contingency coefficient equals 0.42, and Spearman's correlation of the same data is statistically significant ($R=0.33, N=19, p \leq 0.05$), corroborating the previous results.

Partitioning of the ordinal categories above into "Low" versus "Moderate" and "High" impact of the FDA on firm's product strategy, and into "Drug and pharmaceuticals" versus the other products produced the results summarized in Table 17.

Table 17: Impact of the FDA regulations on product strategy of the firm by product area (different grouping)

Impact of the FDA regulations	P r o d u c t a r e a			
	Medical devices and auxiliary products		Drugs or pharmaceuticals with others	
	%	(N)	%	(N)
Low	40	(8)	0	(0)
Moderate or High	60	(12)	100	(6)
Total	100	(20)	100	(6)

Fisher exact test $p \leq 0.081$.

Another way to deal with the FDA constraints might be by decreasing the exposure of the firm to the end-users market, consequently, avoiding to some extent the FDA regulations concerning labeling and advertising. Manufacturing of an intermediate industrial product for original equipment manufacturers (OEMs) or for dealers and wholesalers is a way to operationilize the above objectives.

The data about the sales methods used and their comparative contribution to firm's revenues, presented in Table 18, do not support the above assumption: first, most of the firms use direct sales, which include visits and calls to potential customers. Second, the firms in more regulated product areas use direct methods even more extensively, though the difference is not significant. Although producers of auxiliary products report direct sales to be the main contributors to their revenues, the difference indicated by one-way analysis of variance is still not statistically significant. The data about sales methods that were discarded for some reason are few; only one firm reported that a direct sales method was discarded (medical devices), in comparison to five which discarded indirect methods (4 - medical devices, 1 - auxiliary products).

Table 18: Use of indirect sales and their contribution to firm's revenues by product area

S a l e s m e t h o d s	F r e q u e n c y o f u s e						C o n t r i b u t i o n t o r e v e n u e s					
	P r o d u c t a r e a						P r o d u c t a r e a					
	A u x i l i a r y		D e v i c e s		D r u g s		A u x i l i a r y		D e v i c e s		D r u g s	
	%	(N)	%	(N)	%	(N)	%	(N)	%	(N)	%	(N)
Indirect sales	60	(6)	64	(14)	44	(4)	25	(1)	37	(3)	33	(1)
Direct sales	40	(4)	36	(8)	56	(5)	75	(3)	63	(5)	67	(2)
T o t a l	100	(10)	100	(22)	100	(9)	100	(4)	100	(8)	100	(3)

Note: The distribution above is of those who answered the relevant questions. Up to two sales methods could be reported by each firm.

At this stage we considered the possibility that the data above might be biased due to higher visibility of direct sales, which draw more extensively on entrepreneur's time and effort, in comparison to high volume indirect sales to industrial users. The data in Table 19, concerning the main customer of each firm's product, are somewhat different. Although the trend is not statistically significant (one-way analysis of variance), it is in the hypothesized direction, from more extensive use of direct sales by producers of less regulated product areas such as auxiliary products (86%), to 76% by producers of medical devices, and to 69% by producers of drugs and pharmaceuticals.

Table 19: Sales to industrial customers by product area

Main customers for firm's products	P r o d u c t a r e a					
	Auxiliary products		Medical devices		Drugs and Pharma	
	%	(N)	%	(N)	%	(N)
OEMs and dealers	14	(2)	24	(8)	31	(4)
Direct customers	86	(14)	76	(26)	69	(9)
T o t a l	100	(16)	100	(34)	100	(13)

Note: In our sample there are 6, 14 and 6 firms in each of the above product areas. The number of products in each firm is from 1 to 3.

It is quite clear that the issues of strategic response of the management of biomedical firms to the FDA challenge are very relevant for understanding technological innovation in this industry. Due to the size of the sample and the focus of the study, the data do not allow further analysis of these issues.

The potential impact of new regulations or modifications of existing ones is of sustained concern to policy makers and evaluators of health care products. The products in our sample were launched between 1970 and 1983. The 1976 amendment to the FDA regulation for the first time explicitly included medical devices and other products

and supplies. This created a special opportunity to test its impact in a quasi-experimental setting, though still with only cross-sectional data. We assumed that the new regulations concerning medical devices

Table 20: Schedule of launching new products by biomedical firms in the sample

Year of market entry	First product		Second product		Third product	
	%	N	%	N	%	N
1970-1974	68	17	40	8	25	4
1975-1979	20	6	30	6	19	3
1980-1983	12	3	30	6	56	9
Total	100	26	100	20	100	16

medical devices and their implementation had significant effect on products introduced into the market after 1976. Second, the reported misclassifications, and more arbitrary interpretations of the FDA regulations by the FDA examiners, were probably most intense during the transitory period of 1976-1977, creating a more precarious climate for new products. Third, not only the recently regulated products had been affected by the regulatory changes; at least in two cases, ophthalmological substances (one biological, one synthetic) were initially misclassified as devices, precipitating significant delays in company operations until the right category was found.

To address most of the above issues, we partitioned the sample in several ways. First, we compared the performance of the firms in the sample which launched their first products before 1976 with those who launched them from 1976 and later, with and without those firms whose products were not the target of the new regulations. From the data in Table 21 it is quite clear that the impact of the FDA had been very significant, especially on mobilized resources, and on the scale of operations as represented by the number of employees.

Table 21: Financial and performance indicators and the 1976
FDA amendment

Financial and performance indicators	The whole sample		Excluding drugs and pharma.	
	1st product launched		1st product launched	
	before '76	after '76	before '76	after '76
	N			
Equity (000)	19	7	16	4
Long-term financing (000)	102	11 *	119	16 *
Average sales 1980-83 (000)	1171	469	1369	40 **
Average number of employees first two years	2621	1102	3047	1817
Average number of employees 1980-1983	7	2 **	8	3 *
	54	8 *	62	13 *

T-test of means with separate variances: * $p \leq 0.10$; ** $p \leq 0.05$.

An alternative explanation for the above relations might be the different age of the firms, with older firms launching their products before the younger firms in the sample, concomitantly having more time span for growth and stabilization. This explanation does not hold in the face of the fact that there is no correlation between the age of the firm and the year of launching its first product. In addition, to control for this possibility, but also to reflect the specificity of the transitory period of 1976-77, we divided the sample into three periods: before 1976, 1976-1977, and after 1977.

The results in Table 22 are inconclusive: the financial inputs for the firms which launched their first products in the transitory period are significantly lower than for other firms, but their sales between 1980-1983 are quite high in comparison. Consequently, although the anecdotal evidence provided by the entrepreneurs suggests that the transitory period had had a strong negative influence on their operations the quantitative data do not support it. It should be noted

though that three out of four firms that were dissolved before 1983 launched their first products during this period.

Table 22: Financial and performance indicators and the 1976 FDA amendment; the transitory period of 1976-77

Financial and performance indicators	The whole sample			Excluding drugs and pharma.			
	1st product launched			1st product launched			
	-76	76-77	77+	-76	76-77	77+	
	N	19	3	4	16	2	2
Equity (000)	102	**	6	120	**	7	
Long-term financing (000)	1171	**	93	751	**	0	
Average sales 1980-83 (000)	2622	*	446	3047	*	871	
Average number of employees first two years	7	**	1	8	**	2	
Average number of employees 1980-1983	54	**	4	62	*	7	

T-test of means with separate variances: * $p \leq 0.10$; ** $p \leq 0.05$; the t-test was performed on each pair of means, with its significance specified on the connecting lines. It should be noted here that this procedure of multiple-comparison of means significantly increases the probability of Type I error. The new Type I error = $1 - (1 - p)^2$.

It is interesting to note that the data of the whole sample emphasized the impact of the 1976 amendment on firms whose products had not been its direct target. Those firms still have been affected by the regulatory turmoil and the general industrial climate. When the outliers are excluded the above differences are still statistically significant for the financial inputs and the number of employees at founding and between 1980-1983.

To summarize this section, it should be emphasized that although the data have not always supported the specific hypotheses with statistical significance, they reliably elicited the role of the FDA regulations as a significant constraint for young firms in the

biomedical industry. The implications for technological innovation in this industry are quite unique: the more advanced are the products of the firm, the higher is the risk associated with their use, and consequently, the more articulated is the impact of the FDA regulations on a young firm's strategy, financial requirements, and performance. In the more regulated product areas, such as drugs or medical devices, the economic performance of the firm is significantly more impacted by the FDA. Finally, the impact of the FDA regulations was corroborated by the quasi-experimental setting of the 1976 amendment, which also succeeded in reflecting the impact of regulatory change on the target as well as on other related product areas.

Determinants of success and failure of new biomedical firms

The previous sections have been informative of the relations between the various input factors in the biomedical industry. Some of the data point to causal links between individual level variables, such as educational and professional background of the founders, with the organizational level variables of technological innovation. Other data refer to organizational level processes such as technology transfer, or to corporate strategy stimulated by the challenge of federal regulations. The industry specific issue of interaction between the technological and the clinical product attributes were also comprehensively reviewed.

All these provide only cursory and suggestive information about the central issue of the economic outcomes of the entrepreneurial process and its determinants. Still our data have reliably informed us about several important relations pertaining to economic performance

of biomedical enterprises. On their basis we already know that the educational level of the founders, possibly suggesting applicable knowledge base or skills level, is a strong predictor of firm's performance (Table 4). Firms that had been founded by either MScs or PhDs generated on the average after a decade of operation (1980-1983) 3.7 million dollars of annual sales in comparison to about \$600,000 average sales of firms founded by less formally educated entrepreneurs. Second, the participation of MDs as founders, although very conducive to the technological newness of a firm's products, has inhibited to some extent the economic performance of the firms (Table 6). Third, sustained contacts with the clinical environment, such as hospitals and medical schools, were clearly conducive to technological innovation, and also, to lesser extent, to economic success of the firm (Table 11). In addition, in accord with the Meyer (1982) analysis we found that firms which structured their technological innovation as an evolutionary process, probably focused around a specific core technology, outperformed firms which were less technologically consistent. Finally the 1976 amendment to the FDA regulations has negatively affected subsequent economic performance of biomedical enterprises. Firms which launched their products before 1976 generated on the average about \$1.1 million in annual sales after a decade of operations, in comparison to roughly \$2.6 million by those firms which had more adequately perceived the threats of the regulatory climate. The impact on medical devices and auxiliary products was also more significant than on drugs and pharmaceuticals.

On the basis of these findings, and the data generated by recent research, e.g. Pankiewicz (1980), Taylor (1981), Utterback et

al. (1983), Van de Ven et al. (1983), we proceeded to include considerations of the financial inputs to the firm. At this stage our main objective is to present a more complete picture about the comparative roles of the technological and the financial inputs in influencing economic performance of the young biomedical firm.

The financial attributes of biomedical firms are comparable to other technology-based enterprises studied by Roberts and associates. For instance, Taylor (1981) reported an average of \$67,000 in initial equity and \$48,000 in loans, totaling \$115,000 in initial capital of his industrial "spin-off" firms. In our sample the co-founders and their families provided approximately 62% of this sum, with venture capitalists and banks playing quite a minor role at this initial stage. The subsequent resource mobilization was more substantial, with an average of more than a million dollars in long-term capital, accompanied of course by gradual loss of control of the firm by its

Table 23: Financial profile of biomedical enterprises

Financial parameters of the firm	(N)	R a n g e		Average (\$ 000)
		Minimum (\$ 000)	Maximum (\$ 000)	
Initial equity	(25)	0	850	75
Initial loans	(25)	0	450	56
Total initial capital	(25)	1	1,000	130
Subsequent long-term capital	(24)	0	9,200	1,064*

* Not including the firms that were dissolved, it becomes \$1161K.

initial founders. External ownership increased from 10% to 23% on the average from founding till 1983, with at least five firms having been acquired by biomedical or other conglomerates.

Table 24: Industrial and economic profile of biomedical firms

Industrial and economic parameters (N)	R a n g e		Average
	Minimum	Maximum	
<u>Founding - first 2 years</u> (26)			
Annual sales (\$ 000)	0	918	158
Number of employees	0	37	6
Proportion of exports(%)	0	10	1
<u>1980 - 1983</u> (22)			
Annual sales (\$ 000)	0	24,410	2,490
Number of employees	1	483	50
Proportion of exports(%)	0	30	6

At this stage we cannot ignore the presence of financial outliers in our sample. Two firms, which incidentally have both recently been acquired, had extensive capital financing. The two firms succeeded in mobilizing \$850,000 and a million dollars in initial financing, and their public offerings generated additional \$9.2 and \$6.4 million dollars in equity, respectively. Their economic performances have been accordingly outstanding, with \$30 and \$9 million sales in 1983, averaging \$24.4 and \$7.2 million in annual sales between 1980 and 1983, respectively. In comparison, the total sample's annual sales mean for the same period was about \$2.5 million (for the 22 enterprises which still existed in 1983). These 22 firms generated \$55 million in sales, and about 1100 in employment, with the two outliers contributing approximately 60% to these figures.

These results are not surprising in the face of previous findings about the impact of financial inputs on performance. Our analysis also corroborated the suspicion that the presence of outliers distorts this relation. For instance, the positive Pearson's correlation between the total initial capital and average sales between 1980 and 1983 of $R=0.49$, deteriorates to $R=0.10$ when the

outliers are excluded. The relation between initial capital and firm's estimated market value in 1983 shifts from $R=0.56$ to $R=-0.04$ (!).

Table 25: The relation between financing and performance

Financial Indicators	Performance Indicators							
	Average annual sales 1980 - 1983				Estimated market value in 1983			
	Total sample (N) R		Without outliers (N) R		Total sample (N) R		Without outliers (N) R	
Initial capital	(21)	0.49*	(19)	0.10	(21)	0.56**	(19)	-0.04
Subsequent long-term capital	(22)	0.86**	(20)	-0.13	(22)	0.86**	(20)	0.66**
Pearson correlation * $p \leq 0.05$; ** $p \leq 0.005$.								

A multivariate regression procedure is an adequate summary of our analysis of the relation between the indicators of capital financing and firm's economic performance. The results are quite conclusive in eliciting the effect of the outliers, and the comparative link between initial and subsequent financing, and the economic performance of the firm.

Table 26: Multivariate regression: the relation between initial and subsequent financing and firm's economic performance

Dependent variables Independent variables	Average annual sales 1980 - 1983				Estimated market value of the firm in 1983			
	E x c l u d i n g				E x c l u d i n g			
	Dissolved		Outliers		Dissolved		Outliers	
	BETA	F	BETA	F	BETA	F	BETA	F
Initial capital	0.06	0.2	-0.20	0.6	0.15	1.2	-0.36	3.8
Subsequent long-term capital	0.83	34.1	0.18	0.5	0.78	31.5	0.80	19.0
R square	0.74		0.04		0.75		0.54	
F	25.4		0.4		27.0		9.5	

The second component introduced into our analysis was the intensity of technological innovation activity, measured by its

results in terms of the technological sophistication of firm's products. From Table 27 it is quite clear that the associations between the technological indicators and the estimated market value of the firm between 1977 and 1983 are positive and significant. On the other hand, the relation with average annual sales is somewhat ambiguous: first, the start-up period presents an unstable pattern, with correlations ranging from -0.16 to 0.32 for the three products of the firm, with $R=-0.02$ for products' average. Second, although the correlations between the technological indicators and the annual sales between 1980-1983 are positive and stable, they are still not significant statistically.

In accord with our previous findings it was quite essential to test the above relations for the influence of the two financial-performance outliers. The analysis of the relation between the two input components of capital and technology shows (Table 28) that they are indeed positively and significantly correlated for each of the

Table 27: Technological innovation and economic performance of the firm

Technological Sophistication Indicators for (N)	E c o n o m i c		P e r f o r m a n c e		
	A n n u a l S a l e s		E s t i m a t e d M a r k e t V a l u e		
	First 2 years	1980-83	1977	1980	1983
First product (26)	-0.16	0.18	0.29*	0.26	0.25
Second product (20)	0.28	0.19	0.30*	0.30*	0.24
Third product (16)	0.32	0.27	0.35**	0.37*	0.30
The firm (products' average) (26)	-0.02	0.14	0.31*	0.27*	0.24

Pearson correlation: * $p \leq 0.10$; ** $p \leq 0.05$.

firm's products and for the firm as their average. One way to control for the intervening, and possibly the distorting, impact of the financial variables on the relation between technological innovation

Table 28: Technological innovation and mobilization of financial resources

Technological Sophistication Indicators for (N)	Financial Resources	
	Initial resources equity and loans	Subsequent long-term capital
First product (26)	0.37**	0.31*
Second product (20)	0.37*	0.08
Third product (16)	0.48**	0.12
The firm (products' average) (26)	0.46**	0.21

Pearson correlations: * $p \leq 0.10$; ** $p \leq 0.05$.

and economic performance was to exclude the financing-performance outliers. The results of this procedure speak eloquently for themselves (Table 29): the previous positive relations between the indicators of technological innovation and success become clearly negative for the 20 firms which could not mobilize the necessary "threshold" financing, typical of the two performance outliers.

Table 29: Dimensions of technological innovation and economic performance

Dimensions of technological innovation	Indicators of economic performance of the firm			
	Annual sales 1980-83		Estimated market value 1983	
	E x c l u d i n g		E x c l u d i n g	
	Dissolved (N=22)	Outliers (N=20)	Dissolved (N=22)	Outliers (N=20)
New technology or first of kind	0.17	-0.47**	0.24	-0.35*
Special specifications or purpose	0.06	-0.44**	0.13	-0.33*
Calibre of product or personnel	-0.01	-0.60***	0.11	-0.44**

Pearson correlations: * $p \leq 0.10$; ** $p \leq 0.05$; *** $p \leq 0.01$.

The concept of minimal "threshold" financing, below which the contribution of technological innovation to economic success becomes highly dubious, gains some support from our previous findings pertaining to the impact of the restrictive policy of the FDA. We should bear in mind that this policy has been especially critical to

those firms which attempted to develop and market technologically novel products. Putting it differently, unless the biomedical firm is adequately financed at founding, which in this context means between \$850,000-1,000,000, its technological innovativeness will be detrimental to its economic performance. The mediating role of the risk associated with the use of firm's products, and the problems posed by the FDA "quality assurance" procedure, seem quite plausibly to be an externally imposed handicap on technologically innovative firms.

Additional analyses of data bear upon this issue. First, the correlation between the risk associated with use of a firm's products and its performance indicators is not statistically significant. On the other hand, the more extensively regulated product areas are outperformed by other less regulated areas (Table 30). Although the

Table 30: Average economic performance by firm's product area

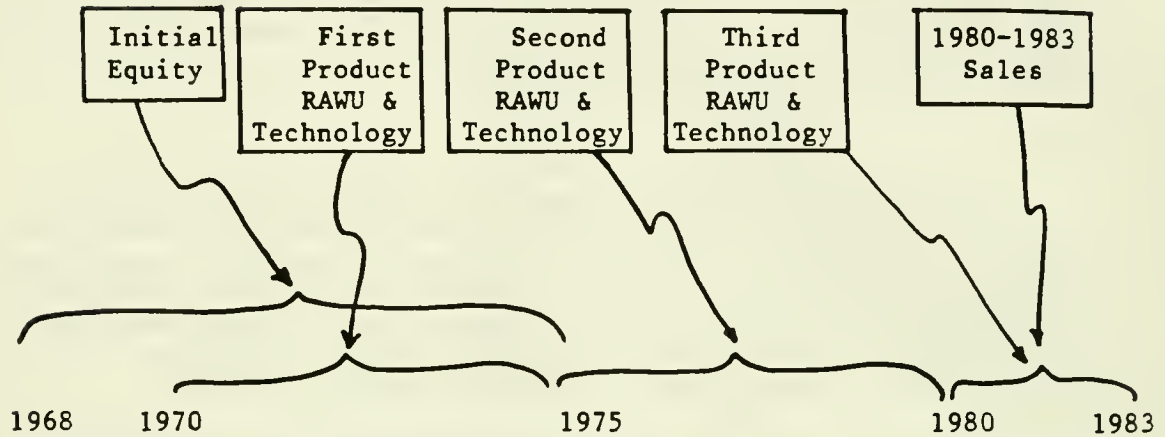
Indicators of economic performance	The sample without firms which had been dissolved			The sample without outliers and dissolved firms		
	Auxiliary N	Medical 4	Drugs & products 13	Auxiliary 4	Medical 11	Drugs & products 5
Annual sales first 2 yrs(\$ K)	239	215	** — 57	239	164	— * — 57
Annual sales 1980-1983 (\$ K)	2,024	3,687	** — 301	2,024	1,391	— ** — 301
Employees first 2 years	3	*	— 8 — ** — 2	3	6	2
Employees 1980-1983	44	67	— * — 7	44	17	7
Initial capital (\$ K)	52	*	— 230 — ** — 49	52	189	— * — 49
Subsequent capital (\$ K)	188	** — 1628	695	188	505	695
Market value 1983 (\$ K)	260	820	160	260	221	160

T-test of means with separate variances: * $p \leq 0.10$; ** $p \leq 0.05$. See note about the influence of multiple-comparison on Type I error, p.58.

firms producing medical devices under the condition of lower than "threshold" initial financing perform better than those producing drugs and pharmaceuticals, they are outperformed by those firms which produce auxiliary products and supplies.

The final step of causal analysis brings together the main potential determinants of economic success of biomedical enterprises - the technological and the financial inputs, and the risk associated with product use (RAWU), which negatively mediates between technological innovation and economic performance. The variables are set in a design which facilitates causal inferences: first, initial financing explicitly precedes the dependent variables of average annual sales between 1980 and 1983, and the estimated 1983 market value of the firm. In addition, the initial financing has been found to be more associated with economic performance than subsequent long-term capital. It should be noted that the causal relation between financing and economic performance can be reversed. Economic performance might increase a firm's credibility, to generate positive speculations about its future; the latter might be exploited by the firm's management to mobilize substantial external capital through public or private offerings. In contrast, the initial capital explicitly precedes in time the 1980-1983 indicators of economic performance, consequently controlling for reversed causality. Second, both the technological innovation and the RAWU measures are based on products which had been launched mainly between 1970 and 1979, with only 29% of them entering the market between 1980 and 1983. The sequence of these events in time is visually described in Figure 3. The formation of these products' attributes took place in the mid-

Figure 3: The time sequence of the variables in the causal model of economic performance of biomedical firms



-seventies and consequently cannot be the outcome of economic performance of the firm between 1980 and 1983.

The results of the regression are indicative of the same process, already elicited through the bivariate inferential analysis. It seems from the regression that initial financing becomes quite inconsequentially related to economic performance when the outliers are excluded. On the other hand, the independent effect of technological innovation on the firm's success is negative and statistically

Table 31: Multivariate regression: determinants of economic performance of biomedical firms

Dependent variables Independent variables	Average annual sales 1980 - 1983				Estimated market value of the firm in 1983			
	E x c l u d i n g				E x c l u d i n g			
	Dissolved BETA	F	Outliers BETA	F	Dissolved BETA	F	Outliers BETA	F
Initial capital	0.60	6.3	0.10	0.2	0.63	7.6	0.20	0.6
Technological sophistication of the firm	-0.15	0.5	-0.60	7.7	-0.05	0.1	-0.49	4.3
Risk associated with use of firm's products	-0.15	0.5	-0.12	0.3	-0.17	0.7	-0.26	1.3
R square	0.28		0.36		0.34		0.26	
F	2.18		2.75		2.90		1.77	

significant; the role of the mediating RAWU is negative, though clearly not significant. There is little difference between the impact of the independent variables on annual sales and market value. Still the explanatory power of the model decreases for annual sales from 34% to 26%, and increases for estimated market value in 1983 from 29% to 36% of their variances.

This analysis suggests that significant technological innovation in biomedical area should be undertaken only by those firms which succeed in securing not less than \$850,000 to a million dollars as initial founding capital. Otherwise the requirements of the product evaluation procedure, enforced by the FDA, will render these attempts at technological innovation economically counterproductive.

Brief agenda for future research

The main contribution of this study was in two areas of the theory of technological innovation. The fact that the similar outweigh the different dimensions in the profiles of biomedical and nonbiomedical entrepreneurs suggests that the theory of technology-based entrepreneurship is empirically well-grounded. Consequently, a meta-analysis of the existing empirical studies in this area is in order and underway by Roberts. It might yield the necessary generalizations, as well as the specifics of internal, external, "spin-off" from either industrial or academic institutions, and biomedical entrepreneurs.

The second area to which this study contributes is the

understanding of the interaction between financial and technological inputs, for externally regulated firms, to determine their economic success. Our results point to the special requirements posed by the regulations-enforcement procedures. On the one hand, the study failed adequately to address the process of corporate strategy formulation and outcomes. The causes of organizational death, not highly represented in our sample, have not been adequately analyzed or understood. The population ecology perspective (Pfeffer & Aldrich, 1976; Hannan & Freeman, 1977) might provide the necessary explanatory power for this issue. Finally, a comparative study of young biomedical firms with the much larger firms of this industry might be quite valuable to elicit their comparative importance for technological innovation, as well as for generation of GNP and employment. Such a comparative study might also address the technological and financial links between small and the large biomedically-oriented firms.

References

- Aldrich, H. E., & Pfeffer, J. (1976). Environments of organizations. Annual Review of Sociology, 2, 79-103.
- Allen, T. J. (1977). Managing the flow of technology. MIT Press, Cambridge, Massachusetts and London, England.
- Allen, T. J., Hyman, Diane B., & Pinckney, David L. (1983). Transferring technology to the small manufacturing firm: A study of technology transfer in three countries. Research Policy, 12, 199-211.
- Allen, T. J., Piepmeier J. M., & Cooney S. (1971). The international technological gatekeeper. Technology Review, 73(5), 5-10.
- Ashford, N. A., Butler, S. E., & Zolt, E. M. (1977). Comment on drug regulation and innovation in the pharmaceutical industry. Unpublished manuscript, Cambridge MA: Center for Policy Alternatives, MIT.
- Bernstein, L. M., Beaven, V. H., Kimberley, J. R., & Moch, M. K. (1975). Attributes of innovation in medical technology and the diffusion process. In Gordon, G., & Fisher, G. L. (Eds.), The diffusion of medical technology, Ballinger Publishing Co., Cambridge, MA.
- Bigelow, B. A. (1982). Innovation in academic medical settings. Unpublished manuscript.
- Buddenhagen, F. L. (1967). Internal entrepreneurship as a corporate strategy for new product development. Unpublished master's thesis, Cambridge MA: MIT Sloan School of Management.
- Coleman, J. S., Katz, E., & Menzel, H. (1966). Medical innovation: A diffusion study. New York, Bobbs-Merrill Co.
- Comroe, J. H., & Dripps, R. D. (1977). The top ten clinical advances in cardiovascular-pulmonary medicine and surgery 1945-1975. U.S. Department of HEW, 1.
- Dorfman, N. S. (1982). Massachusetts' high technology boom in perspective: An investigation of its dimensions, causes, and of the role of the new firms (CPA-82-2). Cambridge MA: Center for Policy Alternatives, MIT.
- Fischhoff, B., Lichtenstein, S., Slovic, P., Derby, S. L., & Keeney, R. L. (1981). Acceptable Risk, Cambridge University Press.
- Food and Drug Administration (1976). Federal Food, Drug, and Cosmetic Act (as amended) October 1976. U.S. Government Printing Office, Washington, DC.

- Forseth, D. A. (1966). The role of government sponsored research laboratories on the generation of new enterprises - a comparative analysis. Unpublished master's thesis, Cambridge, MA: MIT Sloan School of Management.
- Freeman, C. (1965). Research and development in electronic capital goods. National Institute Economic Review, 34, 60-74.
- Fuchs, U. R. (1974). Who shall live? Economics, and social choice, Ch. 6. New York: Basic Books.
- Goldstein, J. (1967). The spin-off of new enterprises from a large government funded industrial laboratory. Unpublished master's thesis, Cambridge, MA: MIT Sloan School of Management.
- Hannan, M. T., & Freeman, J. (1977). The population ecology of organizations. AJS, 82(5), 929-964.
- Hekman, J. S. (1980). Can New England hold onto its high technology industry? New England Economic Review, (March/April), 35-44.
- Homer, J. B. (1983). A dynamic model for analysis of the emergence of new medical technology. Unpublished doctoral dissertation, Cambridge, MA: MIT Sloan School of Management.
- Horwitch, M. (1982). The new complexity in technology innovation and multinational competition: The formation of a multinational biotechnology industry as a case in point. Paper presented at the Conference on Multinationals in Transition, Institute for Research and Information on Multinationals, Paris, France (Nov. 15-16). Revision of Feb. 4, 1983.
- Lawrence, P. R., & Dyer, D. (1983). Renewing American industry. The Free Press, NY.
- Leonard-Barton, D. (1983). Diffusing innovation when the users are not the choosers: The case of dentists (WP #1413-83). Cambridge MA: MIT Sloan School of Management.
- Libby, R., & Blashfield, R. K. (1978). Performance of a composite as a function of the number of judges. Organizational Behavior and Human Performance, 21, 121-129.
- Lieberman, M. B. (1978). A literature citation study of science-technology coupling in electronics. Proceedings of the IEEE in Management of Engineers, G6(1), 5-13.
- Mansfield, E., Romeo, A., Schwartz, M., Teece, D., Wagner, S., & Brach, P. (1982). Technology transfer, productivity, and economic policy. W. W. Norton & Company, NY.
- Martin, A., Reitberger, G., & Utterback, J. with Leonard-Barton, D., Johnson, E., Rao, K. N., & Roberts E. B. (1982) In K. H. Vesper (Ed.), Frontiers of Entrepreneurship Research, Wellesley: Babson College.

- Measday, W. S. (1977). The pharmaceutical industry. In Adams, W. (ed). The structure of American industry. New York: Macmillan.
- Meyer, M. H. (1982). New product strategy in small high technology firms (WP #1382-82). Cambridge MA: MIT Sloan School of Management.
- Moskowitz, J., Finkelstein, S. N., Levy, R.I., Roberts, E. B., & Sondik, E. J. (1981). Biomedical innovation: The challenge and the process. In E. B. Roberts, R. I. Levy, S. N. Finkelstein, J. Moskowitz, & E. J. Sondik (Eds.), Biomedical Innovation (pp. 1-17). Cambridge, MA: MIT Press.
- National Academy of Science (1979). Medical technology and the health care system: A study of diffusion of equipment-embodied technology. National Research Council, Office of Publications, Washington, DC.
- Pankiewicz, R. J. (1974). Determinants of success in technology-based enterprises. Unpublished master's thesis, Cambridge, MA: MIT Sloan School of Management.
- Peters, D. H. (1969). Commercial innovations from university faculty: A study of the invention and exploitation of ideas (WP #406-69). Cambridge MA: MIT Research Program on the Management of Science and Technology.
- Peters, D. H., & Roberts, E. B. (1969). Unutilized ideas in university laboratories. Academy of Management Journal, 12(2), 179-191.
- Roberts, E. B. (1968). A basic study of innovators: How to keep and capitalize on their talents. Research Management, 11(4), 249-266.
- Roberts, E. B. (1981). Influences on innovation: Extrapolations to biomedical technology. In E. B. Roberts, R. I. Levy, S. N. Finkelstein, J. Moskowitz, & E.J. Sondik (Eds.), Biomedical Innovation (pp. 50-74). Cambridge, MA: MIT Press.
- Roberts, E. B., & Peters, D. H. (1981). Commercial innovations from university faculty. Research Policy, 10(2), 108-126.
- Roberts, E. B., & Wainer, H. A. (1971). Some characteristics of technical entrepreneurs. IEEE Transactions on Engineering Management, EM-18(3), 100-109.
- Roberts, E. B., & Wainer, H. A. (1968, December). New enterprises on Route 128. Science Journal, 78-83.
- Rohrbaugh, J. (1979). Improving the quality of group judgment: Social judgment analysis and the Delphi technique. Organizational Behavior and Human Performance, 24, 73-92.
- Rothwell, R., Freeman C., Horsley, A., Jarvis, P., Robertson, A. B., & Townsend, J. (1974). SAPPHO updated - project SAPPHO phase II. Research Policy, 3, 258-291.

- Rubin I., & Wainer, H. A. (1967). Motivation and R&D entrepreneurs: Determinants of company success (WP #234-67). Cambridge MA: MIT Sloan School of Management.
- Schein, E. H. (1978). Career dynamics: Matching individual and organizational needs. Addison-Wesley Publishing Company, Reading, MA.
- Taylor, C. L. (1981). New enterprises descended from a technically based company. Unpublished master's thesis, Cambridge, MA: MIT Sloan School of Management.
- Temin, P. (1979). Technology, regulations, and market structure in the modern pharmaceutical industry. Bell Journal of Economics, 10, 426-446.
- Tilton, J. E. (1971). International diffusion of technology: The case of semiconductors. The Brookings Institute, Washington, DC.
- Utterback, J. M., Reitberger, G., Martin, A., Meyer, M., & Norton, J. (1982). Technology and industrial innovation in Sweden: A study of new technology-based firms (CPA/802-06/A). Cambridge, MA: Center for Policy Alternatives, MIT.
- Van de Ven, A. H., Hudson, R., & Schroeder, D. M. (1983). Designing new business startups: Entrepreneurial, organizational, and ecological considerations. (To be published in Journal of Management).
- Von Hippel, E. (1976). The dominant role of the user in the scientific instruments innovation process. Research Policy, 5(3), 212-239.
- Von Hippel, E. (1977). The dominant role of the user in semiconductor and electronic subassembly process innovation. IEEE Transaction on Engineering Management, EM-24(2), 60-71.
- Von Hippel, E. (1982). Appropriability of innovation benefit as a predictor of the source of innovation. Research Policy, 11(2), 95-115.
- Von Hippel, E., & Finkelstein, S. N. (1978). Product design which encourages or discourages related innovation by users: An analysis of innovation in automated clinical chemistry analysers (WP #1011-78). Cambridge MA: MIT Sloan School of Management.
- Wardell, W. M. (1973). Introduction of new therapeutic drugs in the United States and Great Britain: An international comparison. Clinical Pharmacology and Therapeutics, 14, 773-790.
- Young, J. H. (1982). Public policy and drug innovation. American Institute of the History of Pharmacy, 24, 1-56.

Appendix A: A sample of corporate names selected from the State House directory at Stage 1 ("Phonetic search").

Year of incorporation	C o r p o r a t e N a m e	O b j e c t i v e o f incorporation	Comments
<u>1970</u>	Alpha-Rho Altron Digilab Med-Chem Medical & Technological Inc.	Plastics industry Printed circuits Medical devices Biologicals Medical instruments, marketing only	Excluded Excluded Included Included Excluded
<u>1971</u>	Altec Andonian Cryogenics Cardio-Vascular Inc Gencom Haemonetics	Machine shop Cryogenic equipment Medical devices Telecommunication Medical devices	Excluded Excluded Included Excluded Included
<u>1972</u>	Acta Accudata Cambridge Cyborg Epsilon Med-TAC Orion X-Chrom Supercom Nylamatin	Air pumps Computers Medical instruments Physical research Insurance Detective agency Ophthalmic lenses Metallurgy Electronic machinery	Excluded Excluded Included Excluded Excluded Excluded Included Excluded Excluded
<u>1973</u>	Coronis Ixtlan Teelabco Med-Sil Electronics Trotter Treadmills ADRA N.E. Anasthesia & Instruments	Cafe-restaurant Real estate Medicine, drugs Medical instruments Treadmills only Health club Medical services only	Excluded Excluded Included Included Excluded Excluded Excluded
<u>1974</u>	Chemurgy Micrology Hurlco Health Chroma Comedco Perry Medical Bermed	Chemical consultant Data processing Health food Photo chemicals Medical marketing Medical devices Dental equipment	Excluded Excluded Excluded Excluded Excluded Included Included
<u>1974</u>	BRAX Cardio-pulmonary Technology Preventive Concepts Den-Jay Gamatron Biotherm Mocomo Davicon Nirvana NYPRO	Building materials Medical marketing Health consulting Garment industry Water protection Fuel technology Games Medical devices Restaurant Heat resistant materials	Excluded Excluded Excluded Excluded Excluded Excluded Excluded Included Excluded Excluded

Appendix B: Additional questions specific to the biomedical and the pharmaceutical industry

IIIx-2 Would you describe the nature of your business as directed to development and manufacturing of:

- a) medical devices & instruments _____
- b) pharmaceutical & biological products _____
- c) auxiliary medical or surgical materials and products _____

Please describe briefly:

IIIx-4 For each of your products identified, please evaluate the risk associated with the use of your equipment, devices or drugs according to the following dimensions: (Please check by A(main product), B(2nd product), C(3rd product)):

a) To the medical personnel using it (e.g., due to radiation)	1	2	3	4	5	6	7
	high					negligible	
b) To the patient	1	2	3	4	5	6	7
	high					negligible	
c) To what extent are your products invasive (to the patient)?	1	2	3	4	5	6	7
	very					not at all	
d) Compare your products/ technologies with the products of your key competitors	1	2	3	4	5	6	7
	high						low
	risk						risk

IIIe-2 What were the additional sources of technological knowhow that you have used at your enterprise? Check all which apply, then rank-order them.

Check Rank

Know-how of the founders

Licensing or acquisition of patent rights from:

Universities

Hospitals

_____	_____	R&D firms or individual engineers
_____	_____	Medical firms or individual M.D.s
_____	_____	Foreign
_____	_____	Informal sources (friends and colleagues)
_____	_____	Other (describe) _____

IIIe-3 What are your main continuing technical and medical contacts? Check all which apply, then rank-order them:

<u>Check</u>	<u>Rank</u>	<u>Universities</u>
_____	_____	Medical school at _____
_____	_____	Biological department at _____
_____	_____	Chemical department at _____
_____	_____	Engineering department at _____
_____	_____	Physics department at _____
_____	_____	Other (describe) _____
_____	_____	_____
_____	_____	<u>Hospitals (which?)</u> _____
_____	_____	<u>High-technology companies</u>
_____	_____	<u>R&D, engineering, consulting firms</u>
_____	_____	<u>Government agencies</u>
_____	_____	<u>NIH</u>
_____	_____	<u>Other (describe)</u> _____

SECTION IV -- Influence of FDA Regulations

This section is concerned with the implication of the FDA approval procedure and its influence on operating variables such as budget and schedule.

IV-1 a) If you have developed pharmaceuticals, medicines, biologics and drugs, what are your estimates about the costs and time requirements of the following stages:

	<u>Costs</u>	<u>Time</u>
1. Preclinical tests and reports	_____	_____
2. Phase I tests	_____	_____
3. Phase II tests	_____	_____
4. Phase III tests	_____	_____
5. NDA preparation	_____	_____
6. Post clinical studies	_____	_____

- b) If you have developed biomedical equipment, devices and instruments, what are your estimates about the cost and time requirements of the following stages?

	<u>Cost</u>	<u>Time</u>
1. Class 3 products - clinical tests and reports	_____	_____
2. Change of risk classification of your products from class 3 to class 2	_____	_____

- c) What is the risk classification of your devices, equipment and instruments?

	<u>Number of products</u>
1. Class 1	_____
2. Class 2	_____
3. Class 3	_____

- IV-2 How efficiently has the FDA processed your various reports? State time of processing and number of iterations?

	<u>Time</u>	<u>No. of iterations</u>
a) IND (<u>pharmaceuticals</u>)	_____	_____
b) NDA (<u>pharmaceuticals</u>)	_____	_____
c) 510K (<u>devices</u>)	_____	_____

Remarks _____

- IV-6 Medical and biological research are significantly influenced by specific regulations concerning the test of new devices, drugs and biologics; which of the following regulatory authorities had any impact on your enterprise? Please check.

_____ FDA
 _____ Bureau of Drugs
 _____ Bureau of Biologics
 _____ Bureau of Medical Devices & Diagnostic Products
 _____ Bureau of Radiological Health
 _____ Other Federal (describe) _____
 _____ National Institutes of Health (which?) _____
 _____ State or Local (describe) _____

None

If "none", please go on to question IV-13.

IV-7 In what stages and domains of your entrepreneurial and managerial activities did you consider the above mentioned regulations? Please name the relevant regulatory authority. Check all which apply, then rank order by comparative impact on your activities.

	<u>Check</u>	<u>Rank</u>
a) Initial considerations about starting a new enterprise	_____	_____
b) Financial planning and feasibility studies including the preparation of the business plan	_____	_____
c) Start-up of operations	_____	_____
d) New products planning & development (strategy)	_____	_____
e) New products evaluation and testing	_____	_____
f) Manufacturing and industrial engineering	_____	_____
g) Marketing and advertising	_____	_____
h) Other (describe) _____	_____	_____

IV-8 In what ways did those regulations influence your planning and operations; how many times did these specific events occur during the last 5 years?

	<u>Occurrence in the last five years</u>
1. Had to alter products or process	_____
2. Had to drop products or process	_____
3. Had to develop new products to meet regulation	_____
4. Had to change planned schedules	_____
5. Had to change budget estimates	_____
6. Had to recruit new personnel	_____
7. Had to sell partially developed drug for royalties or lump sum	_____
8. Other (describe) _____	_____

- IV-9 Can you point to cases in which these regulations caused additional expenses and delays in your enterprise? What were the approximate costs and delays?

<u>Situation (describe)</u>	<u>Estimated Delay (months)</u>	<u>Estimated Direct Costs (\$)</u>
1. _____	_____	_____
_____	_____	_____
2. _____	_____	_____
_____	_____	_____

- IV-10 Can you identify any cases in your own enterprise in which the development of a new drug has been launched to overcome these regulatory restrictions? No ___ Yes ___

Describe: _____

- IV-11 Did the uncertainty about possible regulatory requirements alter your planning and operations in any way? No ___ Yes ___
 If yes, describe the situation and your contingency planning for this specific source of uncertainty.

- IV-12 Does your organization include a formal internal review procedure to assess and screen the IND/NDA reports? No ___ Yes ___

Describe it _____

- IV-13 How did you staff and organize to handle the requirements of extensive correspondence and communication with the FDA?

1. During the founding activities _____

2. Full scale operations _____

V-3 Technical innovation achieved by your company since founding:

a) For pharmaceutical/biologicals companies

1. Number of new chemical entities (NCE) _____
2. Number of patents issued _____
3. Number of NCEs tested in man (INDs) _____
4. Number of NCEs submitted for marketing (NDAs) _____
5. Number of NCEs marketed _____
6. Number of publications of employees _____

b) For devices/instruments companies -

1. Number of laboratory prototypes _____
2. Number of production prototypes _____
3. Number of products marketed _____
4. Number of patents issued _____
5. Number of publications of employees _____

Appendix C: Sample attrition statistics (after stage 2)

Cause for Attrition	Total N	Y e a r o f I n c o r p o r a t i o n					
		1970	1971	1972	1973	1974	1975
1. Dental clinic	2						2
2. Not medical	2				2		
3. Only marketing	3				1		2
4. Incorporated too early	5	2	2	1			
5. Not originally incorporated in Massachusetts	1						1
6. Do not want to talk	16	2	3	2	2	1	6
7. No address or contact	47	4	9	10	6	3	15
8. Founder dead	2			1			1
9. Inadequate data	2	1	1				
Total attrition	80	9	15	14	11	4	27
The sample	26	4	4	6	2	5	5
Total set after selection stage 2	106	13	19	20	13	9	32

Appendix D: Sample descriptive dataD-1: Business classification

Business Definition	Frequency			
	1968-1975		1980-1983	
	N	%	N	%
Marketing only	2	8	-	-
Manufacturing only	3	12	3	12
R&D and consulting	4	15	-	-
R&D and manufacturing	6	23	6	23
From R&D to marketing	11	42	17	65
Total	26	100	26	100

D-2: Product area

Product Area	Frequency			
	N	%	N	%
Auxiliary products	6	23	6	23
Medical devices	10	38		
Medical devices and auxiliary products	4	15	14	53
Drugs/pharmaceuticals	3	12		
Drugs/pharmaceuticals and auxiliary products	2	8		
Drugs/pharmaceuticals and medical devices	1	4	6	24
Total			26	100

Appendix E: Criteria and examples for encoding ordinal data

E-1: Type of work, job, position

Encode as "R&D" if work, position, or job was predominantly R&D or research. Encode "Other" for other.

Examples (the first position on the list is the most recent job):

1. Quality assurance, quality assurance, R&D - encode "Other".
2. R&D, self-employed - encode "R&D".
3. R&D, management, self-employed - encode "R&D".
4. R&D, marketing - encode "R&D".

E-2: Type of industry

Encode as "High" if was predominantly university or hospital. Encode "Moderate" if was predominantly medical or pharmaceutical industry. Encode "Low" for other.

Examples(as above):

1. Medical/pharmaceutical industry, and three previous jobs in high-tech industry - encode "Moderate".
2. Three recent jobs in high-tech, previous job in medical/pharmaceutical industry - encode "Low".
3. Chemical industry, university, medical/pharmaceutical industry - encode "Moderate".
4. Hospital, two jobs in high-tech industry - encode "High".

E-3: Sources of product technology

Encode "High" if sources predominantly university, hospitals. Encode "Low" if public domain. Encode "Moderate" if other.

Examples:

1. Government, university/hospital, license - encode "High".
2. Personal experience, public domain - encode "Low".
3. Purchased product line, public domain - encode "Moderate".
4. Personal experience, patent ownership - encode "Moderate".

E-4: Sources of product ideas

(see above - E-3)

E-5: Complementarity of founders' skills

Encode "High" with at least three co-founders with different skills. Encode "Moderate" with at least two different skills. Encode "Low" with either business or technical skills.

Examples:

1. Arts, Sales, MBA, Engineer - encode "High".
2. MBA, Engineer - encode "Moderate".
3. MBA, Sales - encode "Low".
4. Natural Science, MBA - encode "Moderate".

Note: Subsequently was recoded only into two categories of "High" and "Low" complementarity. The former included the original "High" and "Moderate" categories.

Appendix F: Descriptive statistics of RAWUF-1: Distribution statistics of RAWU raw scores

	First Product		Second Product		Third Product	
	N	26		20		16
Statistics		PAT(*) INV(*)		PAT INV		PAT INV
Mean		13.4 14.7		12.8 14.2		14.7 15.1
Median		13.8 16.0		10.5 16.0		14.5 18.0
St Dev		5.5 5.9		6.2 6.4		5.6 6.6
Skewness		-0.3 -0.6		0.1 -0.4		-0.6 -0.8

* PAT = RAWU to the patient; INV = Invasiveness.

F-2: Distribution statistics of RAWU by products, and firm's average

	First Product	Second Product	Third Product	Firm
N	26	20	16	26
Mean	28.2	27.0	29.8	27.9
Median	28.5	28.5	32.5	28.1
St Dev	11.0	12.3	12.1	10.1
Skewness	-0.5	-0.2	-0.7	-0.4

MIT LIBRARIES



3 9080 004 483 357

Date Due

Lib-26-67

BASEMENT

Bar
Code On
Last Page

